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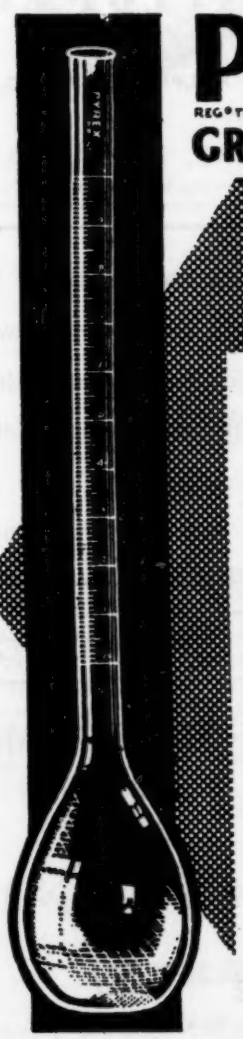

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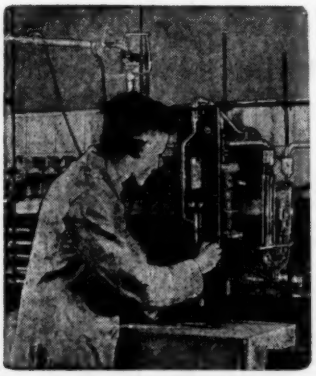

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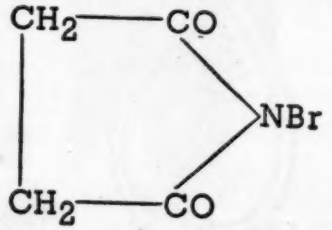

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CONTENTS.

PAPERS COMMUNICATED TO THE CHEMICAL SOCIETY.

General, Physical, and Inorganic.

PAGE

1. The Ternary Systems $NaSCN–Ca(SCN)_2–H_2O$, $KSCN–Ca(SCN)_2–H_2O$, $NH_4SCN–Ca(SCN)_2–H_2O$ and $Ca(SCN)_2–AgSCN–H_2O$ at 25°.
By A. K. McKerrow, V. J. Occleshaw, and (in part) Frank Drabble 1

5. Rare-earth Metal Oxides. Part I. The Direct Oxidation of Praseodymium and Terbium Sesquioxides.
By Joseph K. Marsh 15

6. Rare-earth Metal Oxides. Part II. A New Study of Oxide Precipitation by Nitrate Fusion.
By Joseph K. Marsh 17

7. Rare-earth Metal Oxides. Part III. Their Precipitation from Potassium Hydroxide Melts.
By Joseph K. Marsh 20

8. Studies in the Detoxication of Catalyst Poisons. Part IV. Detoxication of Carbon Disulphide.
By Edward B. Maxted and Arthur Marsden 23

Organic.

2. New Potential Chemotherapeutic Agents. Part III. Derivatives of Diphenylamine and of αα-Diphenylmethylamine.
By F. E. King, T. J. King, and (Miss) I. H. M. Muir 5

3. The Course of Autoxidation Reactions in Polyisoprenes and Allied Compounds. Part XI. Double Bond Movement during the Autoxidation of a Mono-olefin.
By E. Harold Farmer and Donald A. Sutton 10

4. The Acetone Derivatives of Hexahydric Alcohols. Part I. Triacetone Mannitol and its Conversion into *d*-Arabinose.
By L. F. Wiggins 13

9. Retention of Asymmetry During the Beckmann, Lossen, and Curtius Changes.
By A. Campbell and J. Kenyon 25

10. Studies in the Polyene Series. Part XXII. Condensations between Methyl Propargyl Ether and αβ-Unsaturated Carbonyl Compounds.
By I. M. Heilbron, E. R. H. Jones, and R. N. Lacey 27

11. The Constitution of ψ-Santonin. Part I.
By G. R. Clemo and Wesley Cocker 30

12. The Constitution of ψ-Santonin. Part II. The Preparation of Certain Dimethyl Naphthols.
By Wesley Cocker 36

13. Researches on Acetylenic Compounds. Part I. The Preparation of Acetylenic Ketones by Oxidation of Acetylenic Carbinols and Glycols.
By Kenneth Bowden, I. M. Heilbron, E. R. H. Jones, and B. C. L. Weedon 39

14. Researches on Acetylenic Compounds. Part II. (A) The Addition of Amines to Ethynyl Ketones. (B) Auxochromic Properties and Conjugating Power of the Amino Group.
By Kenneth Bowden, Ernest A. Braude, E. R. H. Jones, and B. C. L. Weedon 45

15. Researches on Acetylenic Compounds. Part III. Diene Additions to Ethynyl Ketones.
By Kenneth Bowden and E. R. H. Jones 52

16. Researches on Acetylenic Compounds. Part IV. The Hydration of Some Acetylenylcarbinols Derived From αβ-Unsaturated Aldehydes.
By I. M. Heilbron, E. R. H. Jones, Peter Smith, and B. C. L. Weedon 54

17. Experiments in the Piperidine Series. Part III.
By R. M. Anker and A. H. Cook 58

Notes.—1 : 2 : 3 : 4-Tetrachloronaphthalene.
By W. Palmer Wynne 61

Quinolyl Derivatives of *p*-Aminobenzamide.
By John H. Gorvin 61

The Diethylaminoalkylation of 9-Amino-*p*-phenanthroline.
By Rex G. Jacomb and William O. Kermack 62

Obituary Notices 63

INDEX OF AUTHORS' NAMES.

Anker, R. M., and Cook, A. H., 58.
Bowden, K., Braude, E. A., Jones, E. R. H., and Weedon, B. C. L., 45.
Bowden, K., Heilbron, I. M., Jones, E. R. H., and Weedon, B. C. L., 39.
Bowden, K., and Jones, E. R. H., 52.
Braude, E. A. See Bowden, K.
Campbell, A., and Kenyon, J., 25.
Clemo, G. R., and Cocker, W., 30.
Cocker, W., 36.
Cocker, W. See also Clemo, G. R.
Cook, A. H. See Anker, R. M.
Drabble, F. See McKerrow, A. K.
Farmer, E. H., and Sutton, D. A., 10.
Gorvin, J. H., 61.
Heilbron, I. M., Jones, E. R. H., and Lacey, R. N., 27.
Heilbron, I. M., Jones, E. R. H., Smith, P., and Weedon, B. C. L., 54.
Heilbron, I. M. See also Bowden, K.
Jacomb, R. G., and Kermack, W. O., 62.
Jones, E. R. H. See Bowden, K., and Heilbron, I. M.
Kenyon, J. See Campbell, A.
Kermack, W. O. See Jacomb, R. G.
King, F. E., King, T. J., and Muir, (Miss) I. H. M., 5.
King, T. J. See King, F. E.
Lacey, R. N. See Heilbron, I. M.
McKerrow, A. K., Occleshaw, V. J., and Drabble, F., 1.
Marsden, A. See Maxted, E. B.
Marsh, J. K., 15, 17, 20.
Maxted, E. B., and Marsden, A., 23.
Muir, (Miss) I. H. M. See King, F. E.
Occleshaw, V. J. See McKerrow, A. K.
Smith, P. See Heilbron, I. M.
Sutton, D. A. See Farmer, E. H.
Weedon, B. C. L. See Bowden, K., and Heilbron, I. M.
Wiggins, L. F., 13.
Wynne, W. P., 61.

ERRATA.

Vol., 1945.

Page.	Line.	
728	11*	*for* " *r* " *read* " T ".
731	6	*for* " *acetylmonovinylcarbanilide* " *read* " *monovinylacetylcarbanilide* ".
794	7*	*delete* " and methanol (63 c.c.) ".
795	1	*for* " H_{17} " *read* " H_7 ".
795	33	*for* " 5° " *read* " 50° ".
795	19*	*for* " 40 c.c." *read* " 27 c.c.".
820		in Experimental, l. 3 : *for* " nitrate " *read* " nitrite ".
821	2*	*for* " in addition to anisole, *o*-cresol was formed in small yield whereas at the ordinary pressure *p*-cresol resulted." *read* " the only phenol formed was *o*-cresol, in addition to some anisole ".

* From bottom of text.

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1. *The Ternary Systems* $NaSCN–Ca(SCN)_2–H_2O$, $KSCN–Ca(SCN)_2–H_2O$, $NH_4SCN–Ca(SCN)_2–H_2O$ *and* $Ca(SCN)_2–AgSCN–H_2O$ *at* 25°.

By A. K. McKerrow, V. J. Occleshaw, and (in part) Frank Drabble.

From a study of these condensed ternary systems four new double salts have been found, and the existence of the compound $Ca(SCN)_2,2AgSCN,2H_2O$ confirmed. Some evidence has been obtained showing $Ca(SCN)_2,4H_2O$ to be dimorphous with a transition point at 23·8°. The solubility of calcium thiocyanate from 0° to 50° has been determined.

The isotherms of systems of the type $MSCN–Ba(SCN)_2–H_2O$ in which M was Na, K, NH_4, and Ag have already been studied at 25° (Parts I, II, and III; J., 1931, 55; 1932, 2404; 1934, 1892). We now describe the isotherms at 25° of the four systems in which barium thiocyanate is replaced by the calcium salt. These systems have not previously been investigated. Wells and Merrian (*Amer. Chem. J.*, 1902, **28**, 265) prepared $Ca(SCN)_2,2AgSCN,2H_2O$, the existence of which has now been confirmed, but no double salts between calcium thiocyanate and any of the other three salts are recorded in the literature. The following new double *salts*, all of which are non-congruent, have been found as stable phases: $3KSCN,Ca(SCN)_2,3H_2O$, $2KSCN,Ca(SCN)_2,3H_2O$, $4NH_4SCN,Ca(SCN)_2,2H_2O$, and $7NH_4SCN,6Ca(SCN)_2,12H_2O$. In the system containing the sodium salt anhydrous sodium thiocyanate was found as a stable solid phase. Marked metastability was encountered in the system containing the potassium salt and the following metastable solid phases were observed: $Ca(SCN)_2,2H_2O$, a solid solution with composition approaching that of the double salt $4KSCN,Ca(SCN)_2,2H_2O$, and a second crystalline form of $Ca(SCN)_2,4H_2O$. This result was not unexpected, since $CaCl_2,4H_2O$ exists in three forms (see Bassett *et al.*, J., 1933, 151, who give further references). Throughout this paper the variety of calcium thiocyanate tetrahydrate with the smaller solubility at 25° is referred to as the α-form and the second variety as the β-form. The transition temperature was 23·8°. As a check on this value a small part of the $Ca(SCN)_2,4H_2O$ region in the system containing the silver salt was investigated at 20°, and the β-form recognised as a stable solid phase. Of the other systems, only in the one containing the sodium salt was any attempt made to obtain $\beta\text{-}Ca(SCN)_2,4H_2O$.

Experimental.

Calcium thiocyanate was a good quality commercial sample which was recrystallised from water until the ratio Ca^{2+}/SCN^- was satisfactory. The purification of the sodium and silver salts has already been described (Parts I and II), and the potassium and ammonium salts, which were of "AnalaR" quality, were used without further purification.

Mixtures containing silver thiocyanate were made up as described in Part II, and all other complexes by shaking known proportions of the appropriate salts with definite volumes of water in hard-glass tubes at 25° until a sufficient excess of solid remained. The mixtures were then carefully heated with shaking until solution was complete, and finally rotated in a thermostat regulated at 25° ± 0·05°. The period of shaking depended on the nature of the solid phase and varied from a day, when simple salts alone were involved, to at least a week when dealing with some of the double salts. In previous work on thiocyanate systems metastable conditions were often encountered, and in this work the complexes usually required suitable inoculation to induce crystallisation. In all cases the usual precautions were taken to ensure that a condition of equilibrium had been attained.

Because of the viscous character of the mixtures, the nature of the solid phases was determined by the "residue method." Sintered-glass filters were used to separate the liquid and the solid phases for analysis, all filtrations being carried out at the thermostat temperature. The method of analysis used for the system containing silver thiocyanate is described in Part III. With the other systems, calcium and total thiocyanate were determined, and the amount of the second thiocyanate calculated. Calcium was precipitated as oxalate and then determined volumetrically with standard potassium permanganate solution. In carrying out this determination advantage was taken of the suggestion for washing the precipitate made by Bassett (J., 1934, 1270), and allowance was always made for a blank determination. Total thiocyanate was determined by the Volhard method used under the usual standardised conditions. The ammonium thiocyanate solution used was standardised gravimetrically as the silver salt, and then used to standardise the solution of silver nitrate under the conditions observed in the Volhard method. The concentration of the latter solution was occasionally checked gravimetrically as silver chloride.

All results are expressed as g. per 100 g. of saturated solution or moist solid, and the triangular method of plotting has been used throughout. Broken lines on the diagrams indicate metastability. In several of these systems a microscope was used to confirm the conclusions drawn regarding the nature of the solid phases.

The transition temperature of the two forms of calcium thiocyanate tetrahydrate was determined by three methods: (*a*) thermometrically, (*b*) dilatometrically, (*c*) solubility; the values found were 23·4°, 23·8°, and 23·7°, respectively. In method (*a*) supercooling occurred to a marked degree. With method (*b*) pure Kahlbaum toluene was used as indicator liquid, and the transition point was found from a plot of the rate of volume change against temperature.

Solution		Moist solid.		Solid phase.
NaSCN.	$Ca(SCN)_2$.	NaSCN.	$Ca(SCN)_2$.	
58·78	0	—	—	A
52·08	7·19	64·42	2·16	A
45·37	15·97	61·05	5·65	A
42·98	19·00	58·94	6·46	A
42·99	19·09	72·73	5·89	A, B
m 62·42	0	—	—	B
m 51·47	10·43	—	—	B
m 50·58	11·50	84·50	4·00	B
m 43·83	18·14	90·22	3·06	B
41·74	20·59	82·94	6·74	B
38·82	23·13	81·83	7·39	B
37·91	24·07	82·72	6·88	B
32·38	29·71	69·49	14·10	B
29·32	32·45	80·37	9·22	B
22·40	39·91	76·83	12·28	B
21·32	41·06	—	—	B
19·57	43·27	65·91	18·40	B
16·36	46·46	69·28	16·92	B
14·14	49·67	71·03	17·20	B
11·15	53·03	70·44	17·84	B
11·10	53·52	58·78	24·76	B
9·88	54·48	9·82	59·29	B, C
8·78	55·11	2·75	64·25	C
5·11	57·57	1·15	65·69	C
3·09	58·49	0·68	64·80	C
—	60·20	—	—	C

A = $NaSCN,2H_2O$. B = NaSCN. C = $Ca(SCN)_2,4H_2O$. *m* = Metastable.

System NaSCN–$Ca(SCN)_2$–H_2O (with FRANK DRABBLE).—When the results for this system are plotted, Fig. 1 is obtained. The isotherm consists of the solubility curves of $NaSCN,2H_2O$, NaSCN, and the α-modification of $Ca(SCN)_2,4H_2O$. No solubility curve for the β-form of this salt was found, and there was no indication of double salt formation. In this respect the system resembles the corresponding one containing the barium salt. Fig. 1 shows that anhydrous sodium thiocyanate is stable over a wide area, whereas when barium thiocyanate replaces the calcium salt it occurs only as a metastable phase. In agreement with previous work (de Sweemer, *Natuurwentensch. Tijds.*, 1932, **14**, 231; Parts I and II), no evidence could be found for the existence of the monohydrate of sodium thiocyanate reported by Hughes and Mead (J., 1929, 2282) as being stable below 30·3°, and assumed by Bump (*J. Physical Chem.*, 1932, **36**, 1851). Recalculation of Bump's data to the basis used in this work gives the solubility at 25° as 62·66 g. of NaSCN, and extrapolation of the data given by Hughes and Mead (*loc. cit.*) leads to a value of 62·8 g. It has again been possible to follow the solubility curve of anhydrous sodium thiocyanate throughout the metastable region, the solubility found being 62·42 g. This is in good agreement with the value (62·39 g.) previously found (Part II), and is not far removed from either of the values deduced for this supposed monohydrate.

Sodium thiocyanate crystallises as a dihydrate in long thin needles, which are probably hexagonal, with truncated ends. Bump (*loc. cit.*) describes his monohydrate as long, monoclinic needles. Friend ("Textbook of Inorganic Chemistry," 1924, II, 147) states that the anhydrous sodium salt is rhombic, but the crystals we obtained, though small and poorly formed, appeared to be hexagonal prisms.

Solution.		Moist solid.		Solid phase.
KSCN.	$Ca(SCN)_2$.	KSCN.	$Ca(SCN)_2$.	
70·76	0	—	—	A
66·16	4·01	89·43	1·32	A
59·32	10·51	85·70	3·93	A
53·38	16·78	88·92	3·82	A
49·34	21·41	86·94	5·42	A
45·57	26·61	75·02	12·24	A
44·09	29·16	70·78	15·29	A
43·75	31·39	72·30	15·49	A
43·77	32·21	80·52	11·72	A, B
43·56	31·66	58·75	25·90	
42·84	32·11	50·91	31·70	B
42·07	32·81	51·63	32·15	B
41·12	33·69	51·92	32·28	B
40·22	34·22	54·00	32·15	B
39·06	35·22	47·19	33·63	B
36·89	37·18	51·33	33·03	B
36·28	37·47	43·91	37·20	B, C
m 34·17	39·59	44·47	35·80	B
m 33·53	40·00	46·99	35·23	B
m 31·50	41·61	42·98	37·14	B
m 43·88	32·56	50·07	32·40	A, C
m 42·81	33·38	46·05	37·04	C
m 41·91	34·61	44·83	37·48	C
m 38·80	36·01	45·30	38·23	C
35·39	37·95	42·55	38·31	C
32·56	40·17	43·48	39·41	C
26·55	44·66	39·57	41·08	C
24·00	46·65	39·92	41·11	C
18·62	51·82	31·11	46·25	C
17·77	53·18	21·20	53·62	C, α-D
m 21·32	52·10	9·18	61·18	α-D
17·54	53·19	9·52	60·05	α-D
13·81	54·39	8·13	59·95	α-D
10·46	55·68	5·65	61·22	α-D
7·90	56·67	4·61	61·65	α-D
5·23	57·71	2·36	63·83	α-D
2·13	58·99	1·04	63·81	α-D
0	60·20	—	—	α-D
m 13·76	54·56	6·46	61·63	β-D
m 10·56	55·89	3·84	63·46	β-D
m 6·40	57·63	2·52	64·25	β-D
m 4·68	58·60	1·40	67·90	β-D
m 2·77	59·55	0·47	66·30	β-D
mx 0	61·10	—	—	β-D
my 0	60·75	—	—	β-D
m 43·75	33·61	56·63	28·98	A, E
m 41·83	35·31	51·41	32·12	E
m 40·38	36·34	56·35	30·94	E
m 36·74	39·52	51·16	33·96	E
m 32·60	43·96	49·82	36·15	E
m 29·05	48·50	44·44	41·39	E
m 28·30	49·57	28·92	55·25	E, F
m 28·49	49·20	20·25	58·51	F
m 25·26	50·82	14·90	63·37	F
m 23·46	52·14	9·37	66·34	β-D, F

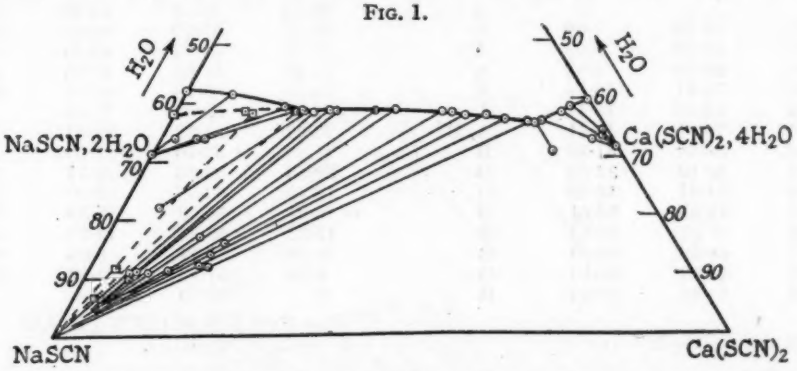
A = KSCN.
B = $3KSCN,Ca(SCN)_2,3H_2O$.
C = $2KSCN,Ca(SCN)_2,3H_2O$.
E = Solid solution approaching $4KSCN,Ca(SCN)_2,2H_2O$.

m = Metastable.
x = Estimated from Fig. 2*b*.
α-D, β-D = $Ca(SCN)_2,4H_2O$.
F = $Ca(SCN)_2,2H_2O$.
y = Estimated from data on p. 5.

System KSCN–$Ca(SCN)_2$–H_2O.—To avoid overcrowding, only a selection of the results has been plotted to give the composite Fig. 2. The stable isotherm is made up of four solubility curves corresponding to the solid phases KSCN, $3KSCN,Ca(SCN)_2,3H_2O$, $2KSCN,Ca(SCN)_2,3H_2O$, and $Ca(SCN)_2,4H_2O$ (Fig. 2*a*). In addition, the diagram shows solubility curves for the three metastable solid phases already mentioned (Figs. 2*a* and 2*b*), and indicates that it was possible to follow the solubility curve of $3KSCN,Ca(SCN)_2,3H_2O$ into the metastable region with increasing concentration of calcium thiocyanate, and to prolong the solubility curve of the other stable double salt to its metastable invariant with

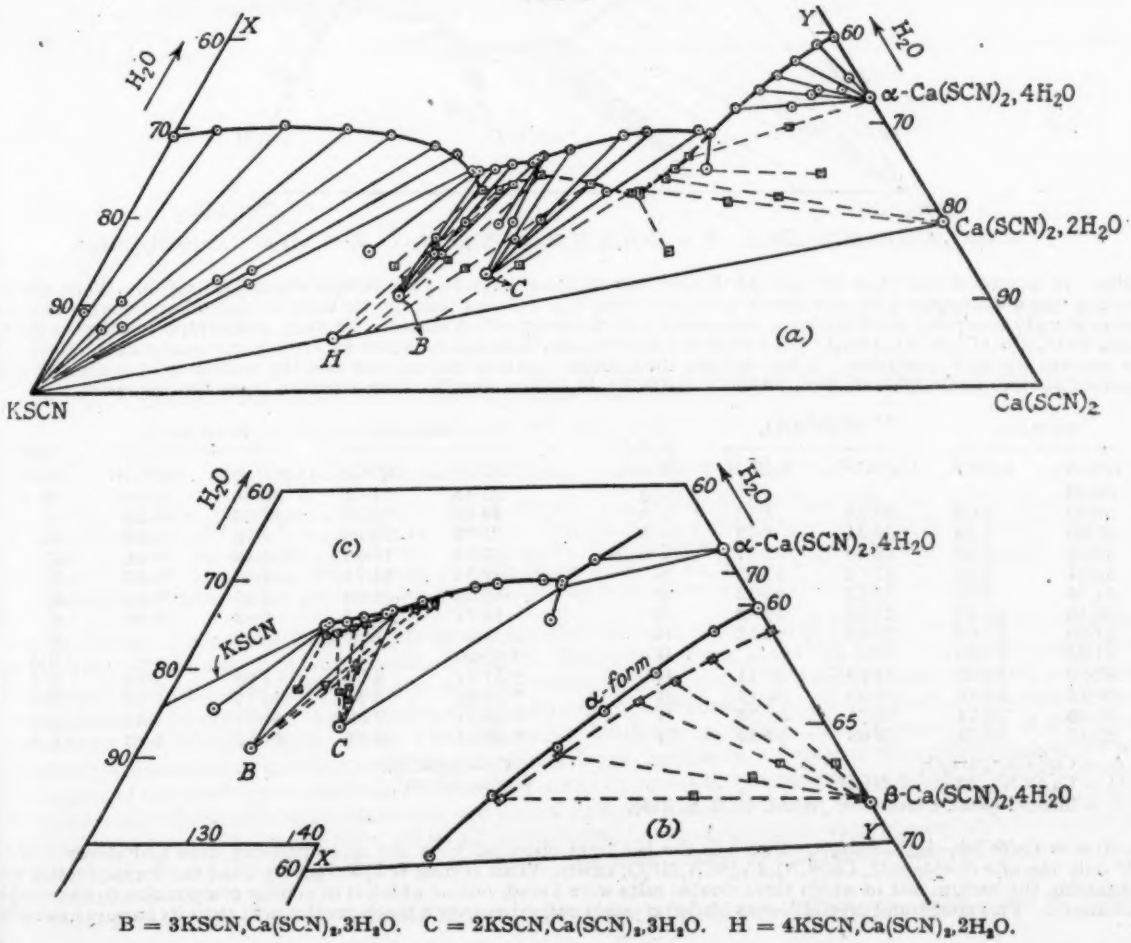
potassium thiocyanate (Fig. 2*c*). The corresponding system containing the barium salt was not so complex and contained only one double salt, *viz.*, 3KSCN,2Ba(SCN)$_2$,5H$_2$O, showing no analogy with either of those now reported.

FIG. 1.



Potassium thiocyanate crystallises as long, thin, ill-defined needles, and the compound 3KSCN,Ca(SCN)$_2$,3H$_2$O as needle-like crystals which are six- or more-sided and brachydomal. The other stable double salt, 2KSCN,Ca(SCN)$_2$,3H$_2$O, separated as thin rectangular plates, occasionally associated with square ones; the solid solution was obtained as thin hexagonal plates, and dihydrated calcium thiocyanate crystallised as hexagonal prisms with basal pinacoid and length 4—8 times the breadth. The α-form of tetrahydrated calcium thiocyanate was obtained as ill-defined rhombs, and the β-form appeared as hexagonal needles with pyramidal ends. Added potassium thiocyanate seemed to exert a stabilising influence on the β-form. As it was not possible to obtain this form at 25°, without addition of about 5% of the potassium salt, its solubility above the transition temperature could only be estimated from its solubility curves by extrapolation. Unmack, Murray-Rust, and Hartley (*Proc. Roy. Soc.*, 1930, *A*, **127**, 228) obtained calcium thiocyanate dihydrate by dehydration of the tetrahydrate, and we have confirmed their observation that attempts to dehydrate it, even at room temperature, result in decomposition.

FIG. 2.



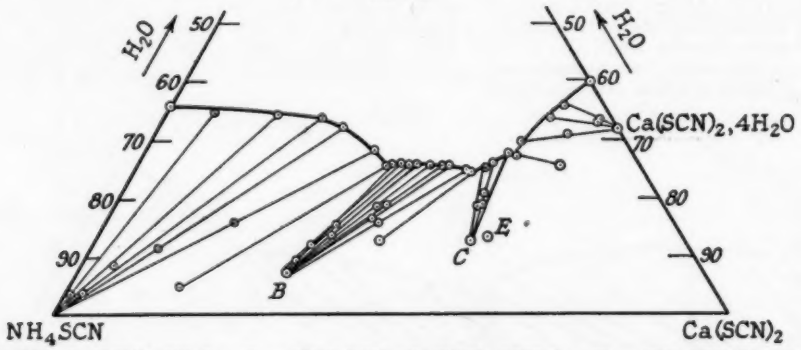
B = 3KSCN,Ca(SCN)$_2$,3H$_2$O. C = 2KSCN,Ca(SCN)$_2$,3H$_2$O. H = 4KSCN,Ca(SCN)$_2$,2H$_2$O.

Solution.		Moist solid.		
NH_4SCN.	$Ca(SCN)_2$.	NH_4SCN.	$Ca(SCN)_2$.	Solid phase.
64·33	0	—	—	A
57·85	7·29	95·54	1·09	A
49·18	16·70	86·52	5·00	A
42·72	23·62	93·53	2·83	A
40·38	27·52	78·61	10·14	A
37·84	34·00	64·68	19·44	A
37·67	37·01	78·81	16·41	A, B
36·98	37·36	58·56	31·85	B
35·04	39·04	55·40	32·53	B
34·35	39·49	54·91	32·28	B
34·13	40·19	49·89	34·61	B
32·89	41·58	51·37	34·83	B
31·48	43·22	48·28	36·69	B
31·37	43·29	42·43	39·18	B
29·04	45·33	40·84	40·58	B
28·15	46·24	44·30	39·40	B
26·87	47·29	42·68	40·70	B
25·95	49·07	43·39	40·89	B
25·50	49·89	41·16	43·01	B, C
25·55	50·13	45·06	42·07	B, C
24·45	50·99	28·15	53·34	C
23·31	51·62	27·51	53·78	C
21·38	52·76	25·50	54·04	C
20·55	53·26	25·77	53·68	C
18·40	53·95	26·50	54·53	C
m 16·91	55·22	23·59	55·72	C
17·32	55·64	11·74	62·69	C, D
15·23	55·11	8·01	61·24	D
9·29	57·14	2·19	65·15	D
0	60·20	—	—	D

A = NH_4SCN.
B = $4NH_4SCN,Ca(SCN)_2,2H_2O$.
m = Metastable.
C = $7NH_4SCN,6Ca(SCN)_2,12H_2O$.
D = $Ca(SCN)_2,4H_2O$.

System NH_4SCN–$Ca(SCN)_2$–H_2O.—Fig. 3 has been constructed from the accompanying results, with the addition of the point representing the compound $NH_4SCN,Ca(SCN)_2,2H_2O$. There are four branches to the isotherm which includes solubility curves for the double salts $4NH_4SCN,Ca(SCN)_2,2H_2O$ and $7NH_4SCN,6Ca(SCN)_2,12H_2O$ and the two simple

FIG. 3.



= $4NH_4SCN,Ca(SCN)_2,2H_2O$. C = $7NH_4SCN,6Ca(SCN)_2,12H_2O$. E = $NH_4SCN,Ca(SCN)_2,2H_2O$.

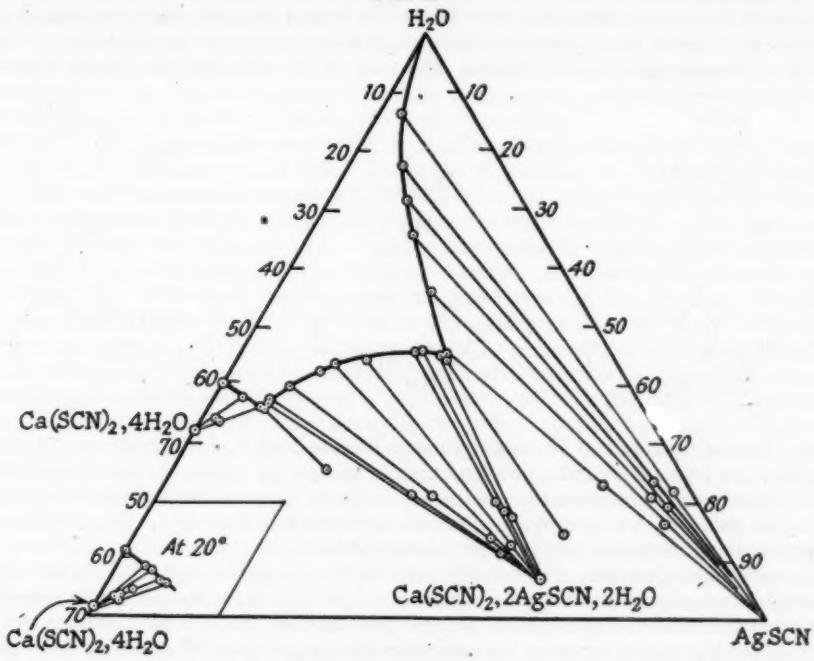
salts. It is improbable that the second double salt is being mistaken for $NH_4SCN,Ca(SCN),2H_2O$. Work on this system was not hampered by metastable conditions and Fig. 3 shows that the tie lines for this second double salt converge sharply to a point representing a compound with the composition stated. Further, points representing the double salts $7NH_4SCN,6Ca(SCN)_2,12H_2O$ and $NH_4SCN,Ca(SCN)_2,2H_2O$ are too far apart for error in the analytical method used to account for such confusion. When barium thiocyanate replaces the calcium salt the system is of a simpler type, containing but one double salt, *viz.*, $NH_4SCN,Ba(SCN)_2,H_2O$, less complex than either of those now reported.

Solution.		Moist solid.		
$Ca(SCN)_2$.	AgSCN.	$Ca(SCN)_2$.	AgSCN.	Solid phase.
60·20	—	—	—	α-A
58·80	4·03	66·13	1·73	α-A
57·05	7·49	64·31	2·73	α-A
57·03	7·52	52·00	22·67	α-A, B
55·21	8·50	41·14	37·53	B
54·74	8·26	33·52	55·33	B
50·76	10·27	38·43	40·62	B
44·99	13·09	32·54	53·43	B
41·95	14·96	—	—	B
37·02	19·22	31·00	56·11	B
29·12	25·71	29·59	50·17	B
27·86	26·74	29·34	52·26	B
25·47	29·79	28·63	54·10	B
25·15	31·01	22·58	63·08	B, C
24·52	30·70	12·56	64·39	C
21·72	22·88	6·75	76·88	C
19·23	15·42	6·23	72·76	C
17·33	11·74	4·80	75·97	C
15·01	8·09	4·69	75·85	C
14·11	3·42	2·82	75·30	C
x —	0·00002	—	—	C
* 59·00	—	—	—	β-A
* 57·27	4·24	64·60	2·15	β-A
* 56·85	5·19	63·75	2·72	β-A
* 56·41	7·50	60·95	4·54	β-A
* 55·44	8·73	64·57	3·02	β-A

A = $Ca(SCN)_2,4H_2O$.
B = $Ca(SCN)_2,2AgSCN,2H_2O$.
x = Masaki (*Bull. Chem. Soc. Japan*, 1930, **5**, 345).
C = AgSCN.
* = At 20°.

System $Ca(SCN)_2$–AgSCN–H_2O.—Fig. 4 is the isotherm obtained from the accompanying data and shows that at 25° only the one double salt, $Ca(SCN),2AgSCN,2H_2O$, exists. This system is less complex than the corresponding one containing the barium salt in which three double salts were found, one of which is of similar composition to the double salt above. This compound crystallises as bladed crystals and exists over a much greater area than its barium analogue.

FIG. 4.



Further, the solubility curve of $Ca(SCN)_2,4H_2O$ is comparatively short. The data include a few results obtained for this system at 20°.

Solubility of Calcium Thiocyanate.—The following results were obtained for the solubility (S) at various temperatures.

β-Form.

Temp.	0°	8°	16°	20°	23°	25°	25°
S	55·44	56·11	57·90	59·00	59·80	60·75 *	61·10 *

α-Form.

Temp.	25°	27·5°	30°	35°	41°	45°	50°
S	60·20	60·26	60·54	60·94	61·69	62·37	63·27

* See p. 2.

From these results the transition temperature, 23·7°, was obtained.

LIVERPOOL UNIVERSITY. [*Received, September 22nd*, 1945.]

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2. *New Potential Chemotherapeutic Agents. Part III. Derivatives of Diphenylamine and of αα-Diphenylmethylamine.*

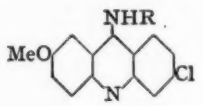
By F. E. KING, T. J. KING, and (MISS) I. H. M. MUIR.

The existence in mepacrine (I, R = $CHMe{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}NEt_2$) of the diphenylamine and αα-diphenylmethylamine ring-systems suggested that similarly substituted derivatives of these more accessible amines might also possess antimalarial properties. Compounds of the type (II, R = $CH_2{\cdot}CH_2{\cdot}NEt_2$) and (III, R = $CH_2{\cdot}CH_2{\cdot}NEt_2$), including certain pyrimidine analogues, *e.g.* (VI, R = $NH{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}NEt_2$), were therefore synthesised, but neither series has afforded any substances of chemotherapeutic interest.

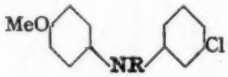
THE evolution of synthetic antimalarial agents was the outcome of a series of largely empirical investigations originating with the work of Guttmann and Ehrlich (*Berlin klin. Woch.*, 1891, **28**, 953). Their discovery of the antimalarial properties of methylene blue was later followed by the observation that more effective compounds were obtainable by replacing the normal substituents of the dyestuff with certain *basic* alkyl groups (Schulemann, Schönhöfer and Wingler, *Klin. Woch.*, 1932, **11**, 381). With the recognition of the importance of the amino-alkylamine side-chain as a constituent of antimalarial drugs, further developments were chiefly concerned with variations of the heterocyclic nucleus, and the discovery of pamaquin (plasmoquin) was based on the knowledge that the naturally occurring antimalarials are quinoline derivatives. Finally, in seeking a series of less toxic character, Mauss and Mietzsch (*ibid.*, 1933, **12**, 1276) found in the acridine derivative, mepacrine hydrochloride (atebrin), (I, R = $CHMe{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}NEt_2,2HCl$), the most effective suppressive and prophylactic agent yet described.

Although the researches on mepacrine have led to the preparation of numerous derivatives of acridine,

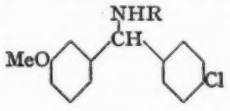
little attention has been given to the investigation of similarly substituted compounds of a somewhat simplified structure. In view of the many instances now known in which similar pharmacological properties persist throughout a series of compounds of comparatively superficial structural resemblance, it seemed of interest to examine certain of these mepacrine analogues. The nucleus (I) embodies the ring-systems of two relatively



(I.)



(II.)



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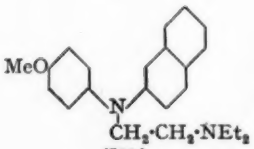

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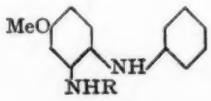

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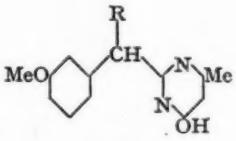

(VI.)

simple amines, *viz.*, diphenylamine and αα-diphenylmethylamine, and their derivatives, (II) and (III), in which R denotes the customary basic side-chain, are structurally analogous to mepacrine. Experiments were therefore undertaken to synthesise representative examples of these types. As in Parts I and II, instead of the normal mepacrine side-chain, we have employed the basic substituents $Et_2N{\cdot}CH_2{\cdot}CH_2-$ and $Et_2N{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2-$ on account of the greater accessibility of the appropriate alkylating agents.

The alkylation of diphenylamines, a necessary step in the preparation of the series represented by (II, R = $CH_2{\cdot}CH_2{\cdot}NEt_2$), is usually effected by the action of alkyl halides on their *N*-sodio compounds (Titherley, *J.*, 1897, **71**, 465). Preliminary experiments on the preparation of *N*-β-diethylaminoethyldiphenylamine indicated that it is probably more convenient to alkylate the magnesium salt obtained from the diphenylamine and methylmagnesium iodide (cf. Oddo, *Gazzetta*, 1911, **41**, 255), and the synthesis of N-β-*diethylaminoethyl*-4-*methoxydiphenylamine* by both methods confirmed this observation. The preparation of 4-methoxydiphenylamine by the usual Ullmann method (Wieland and Wecker, *Ber.*, 1910, **43**, 708) gave a cleaner product when the monomethylnaphthalenes replaced nitrobenzene as solvent, possibly because of the oxidising properties of the latter in presence of the alkali.

The substituted diphenylamine of the required orientation (II, R = $CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}NEt_2$) was prepared from *m*-chloronitrobenzene, which was hydrogenated in the presence of Raney nickel to the *m*-chloroaminobenzene, characterised by the p-*toluenesulphonamide*. This amine was used as a source of *m*-chloroiodobenzene which was condensed with acetyl-*p*-anisidine, and the resulting *N*-acetyldiphenylamine was hydrolysed without isolation to 3-*chloro*-4′-*methoxydiphenylamine* (II, R = H). Alkylation through the amine magnesium iodide afforded the *N*-β-diethylaminoethyl compound (II, R = $CH_2{\cdot}CH_2{\cdot}NEt_2$) which gave a crystalline *oxalate* and *hydrochloride*. A somewhat similar compound of higher molecular weight, (IV), was prepared from 4-methoxyphenylnaphthylamine and β-chloroethyldiethylamine and was characterised by its *hydrochloride*.

2-*Nitro*-4-*methoxydiphenylamine* was also prepared by the Ullmann reaction for the synthesis of (V, R = $CH_2{\cdot}CH_2{\cdot}NEt_2$), in which the substituents have the pamaquin orientation. It was necessary in this preparation to use *N*-acetyl-3-nitroanisidine, bromobenzene and activated copper; the method which Kehrmann and Havas (*Ber.*, 1913, **46**, 341) employed for 2-nitrodiphenylamine failed when applied to 4-bromo-3-nitroanisole and acetanilide, the mesomeric effect of the methoxyl on the bromine atom opposing that of the activating *o*-nitro group. Reduction of the nitrodiphenylamine in the presence of Raney nickel gave the readily oxidisable 2-*amino*-4-*methoxydiphenylamine* (V, R = H), but this could not be made to react with β-chloroethyldiethylamine under the usual conditions. An attempt to alkylate the 2-*N*-sodio compound after acetylation of the reactive secondary nitrogen atom gave 5-*methoxy*-1-*phenyl*-2-*methylbenziminazole* as the sole product. When the 2-p-*toluenesulphonyl* derivative (V, R = $p{\cdot}SO_2{\cdot}C_6H_4{\cdot}Me$) was alkylated with γ-chloropropyldiethylamine in presence of sodamide, 2-p-*toluensulphon*-(γ-*diethylaminopropyl*)-*amido*-4-*methoxydiphenylamine* was obtained as a crystalline solid. This appeared to resist the action of sulphuric acid, and when the protecting group was removed by sodium in liquid ammonia, admission of air so rapidly oxidised the product that its isolation proved impracticable.

The synthesis of (III, R = $CH_2{\cdot}CH_2{\cdot}NEt_2$) was modelled on that of the simple N-β-*diethylaminoethyl*-αα-*diphenylmethylamine*, $Ph_2CH{\cdot}NH(CH_2)_2{\cdot}NEt_2$, which was obtained by alkylation of αα-diphenylmethylamine or of its magnesium derivative, $Ph_2CH{\cdot}NHMgI$, with β-chloroethyldiethylamine. αα-Diphenylmethylamines are conveniently prepared from the appropriate benzophenones by heating with ammonium formate (Leuckart and Bach, *Ber.*, 1886, **19**, 2129), the resulting *N*-formyl derivatives being hydrolysed with acid. The chloromethoxybenzophenone of the required orientation was obtained from 4-chloro-3′-nitrobenzophenone which was reduced by stannous chloride in alcoholic hydrochloric acid to the 3-*amino* compound, and thence converted by diazotisation and heating to 4-*chloro*-3′-*hydroxybenzophenone*. Methylation to the *methoxybenzophenone* was achieved with either methyl sulphate and sodium methoxide or methyl iodide and potassium carbonate in methanol. Application of the Leuckart reaction, using the modified conditions of Ingersoll *et al.* (*J. Amer.*

Chem. Soc., **1936**, **58**, 1809), gave *4-chloro-3'-methoxy-αα-diphenylamine* (III, R = H), and alkylation through the Grignard compound led to the amine (III, R = $CH_2 \cdot CH_2 \cdot NEt_2$). At the same time *N-β-diethylaminoethyl-4-chloro-4'-methoxy-diphenylmethylamine* was synthesised by similar methods, the required benzophenone being obtained by the action of *p*-chlorobenzoyl chloride on anisole (Peterson, *ibid.*, **1924**, **46**, 339). The *dihydrochloride* was highly crystalline, but the corresponding salt of the homologous γ-diethylaminopropylamine, obtained from the purified *dioxalate*, could not be obtained in a crystalline state.

Hydrochlorides of the foregoing amines were tested against trophozoite infections of (a) *P. relictum* in canaries, at the Molteno Institute, Cambridge, and/or (b) *P. gallinaceum* in chicks, at the National Institute for Medical Research, London, but with the doubtful exception of (III, R = $CH_2 \cdot CH_2 \cdot NEt_2$), they exerted no antimalarial action. A possible explanation for their failure was that, unlike their prototype, these new derivatives did not possess a heterocyclic nucleus, and this led us to consider the synthesis of analogues containing a heterocyclic radical in place of one of the aryl groups. Of several alternatives, the pyrimidine nucleus was selected, first, because of the relative ease with which the necessary intermediates can be prepared, and secondly, in view of the widespread occurrence of pyrimidines as constituents of living cells, the introduction of a pyrimidine ring was not likely to give rise to unduly toxic compounds. The preparation by Pinner (*Ber.*, **1891**, **23**, 2948) of 4-hydroxy-2-(α-hydroxybenzyl)-6-methylpyrimidine, derived from mandelonitrile by condensation of the related amidine with ethyl acetoacetate, suggested a practicable route to the desired compounds. The crude cyanohydrin from *m*-methoxybenzaldehyde was rapidly transformed by the action of hydrogen chloride in ether–methanol into the methyl imino-ester *hydrochloride*, and this with alcoholic ammonia was converted into the amidine *hydrochloride*; the latter, by condensation with ethyl acetoacetate in alcoholic alkali, gave *4-hydroxy-2-(α-hydroxy-*m*-methoxybenzyl)-6-methylpyrimidine* (VI, R = OH). Replacement of the α-hydroxy group occurred on treatment with thionyl chloride in cold chloroform to give the corresponding *α-chloro* compound, a crystalline solid which reacted with α-diethylaminopropylamine forming the pyrimidine (VI, R = $NH \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot NEt_2$). This was identified by its *dipicrate* and *dipicrolonate*, but the amine hydrochloride obtained from the latter by treatment with the aqueous acid could not be obtained crystalline.

From *o*-chlorobenzaldehyde the analogous series of *o*-chloro compounds has been similarly prepared, and the final product, *4-hydroxy-2-[α-(γ-diethylaminopropyl)amino-o-chlorobenzyl]-6-methylpyrimidine* characterised by its crystalline *dipicrolonate* and deliquescent *hydrochloride*. Neither the methoxy- nor chloro-γ-diethylaminopropylaminopyrimidine hydrochlorides showed any activity against trophozoite infections of *P. gallinaceum* in chicks.

Experimental.

N-β-Diethylaminoethyldiphenylamine.—A solution prepared from magnesium (1 g., *ca.* 1·5 mol.), methyl iodide (6·2 g.) and ether (20 c.c.) was slowly treated in a hydrogen atmosphere with diphenylamine (5·2 g., 1 mol.) in benzene (100 c.c.) and refluxed for 30 minutes. To the boiling liquid, β-chloroethyldiethylamine (5·9 g., 1·25 mol.) dissolved in benzene (10 c.c.) was then added in 3 portions during 1 hour, and after a further 1½ hours the mixture was cooled and shaken with aqueous ammonium chloride. The 10% hydrochloric acid extract of the benzene layer was made alkaline and the liberated amine isolated by means of ether. *N-β*-Diethylaminoethyldiphenylamine, a straw-coloured oil (2 g., 31%), b. p. 145°/0·15 mm., gave a *picrate* which separated from alcohol in needles, m. p. 142—145° (Found: C, 57·6; H, 5·5. $C_{18}H_{24}N_2,C_6H_3O_7N_3$ requires C, 57·9; H, 5·4%).

N-β-Diethylaminoethyl-4-methoxydiphenylamine.—Only poor yields of discoloured product were obtained in the preparation of 4-methoxydiphenylamine from acet-*p*-anisidide, bromobenzene, potassium carbonate and copper-bronze in refluxing nitrobenzene (Wieland and Wecker, *loc. cit.*), but with α- and β-methylnaphthalenes as solvent, the methoxydiphenylamine was obtained after distillation at 160°/0·4 mm. as an orange solid (yield 75%), m. p. 105°.

The sodium salt obtained by cautiously heating a powdered mixture of 4-methoxydiphenylamine (10 g., 1 mol.) and sodamide (5 g., 2·5 mol.), finally to 200° (Titherley, *loc. cit.*), was covered with benzene (150 c.c.), and to the refluxing liquid a solution of β-chloroethyldiethylamine (8 g., *ca.* 1·2 mol.) in benzene (20 c.c.) was added. After 4 hours' heating, in a hydrogen atmosphere, the base extracted from the solvent by 10% hydrochloric acid was distilled. The *N*-alkyldiphenylamine, a pale orange oil (2·5 g., 16·7%) which darkened in air, had b. p. 180°/0·15 mm., and gave a *picrolonate* which separated from alcohol in yellow needles, m. p. 120—121° (Found: C, 61·5; H, 6·2. $C_{19}H_{26}ON_2,C_{10}H_8O_5N_4$ requires C, 61·9: H, 6·1%).

The reagent prepared from magnesium (1·6 g.), methyl iodide and ether was treated with 4-methoxydiphenylamine (13 g.) dissolved in benzene (110 c.c.) and heated for 2½ hours with β-chloroethyldiethylamine (13 g.). When the product was worked up as in the case of *N*-diethylaminoethyldiphenylamine, the 4-methoxy analogue, b. p. 145—155°/0·07 mm., was obtained and gave a *picrate* crystallising in orange prisms, m. p. 139° (Found: C, 56·5; H, 5·5. $C_{19}H_{26}ON_2,C_6H_3O_7N_3$ requires C, 56·8; H, 5·5%). The purified salt dissolved in a little alcohol was treated with concentrated hydrochloric acid, and when the picric acid had been removed with ether, the amine was recovered by addition of alkali and distillation. From a dry ethereal solution of the product hydrogen chloride precipitated the *hydrochloride* (2·5 g.) which crystallised from alcohol in colourless needles, m. p. 130° (Found: C, 68·5; H, 7·9. $C_{19}H_{26}ON_2,HCl$ requires C, 68·2; H, 8·1%).

m-Chloroaniline.—*m*-Chloronitrobenzene (30 g.) dissolved in ethanol (100 c.c.) was rapidly reduced in presence of Raney nickel (2·5 g.) at room temperature and 2—3 atm., giving the chloroaniline (24 g., 98·5%), b. p. 113°/18 mm. *p-Toluenesulphon-3-chloroanilide* crystallised from alcohol in colourless needles, m. p. 134° (Found: C, 55·5; H, 4·4. $C_{13}H_{12}O_2NClS$ requires C, 55·4; H, 4·3%).

3-Chloro-4'-methoxydiphenylamine (II, R = H).—A mixture of acet-*p*-anisidide (30 g., 1 mol.), *m*-chloroiodobenzene (69 g., 1·6 mol.), potassium carbonate (14 g., 1·1 mol.) and copper-bronze (0·8 g.) was heated in refluxing nitrobenzene (160 c.c.) for 32 hours with exclusion of air. Steam-distillation followed by heating the residue with hydrochloric acid (12%, 120 c.c.) gave a product which was dissolved in ether and twice passed through a charcoal column. Distillation gave the chloromethoxydiphenylamine, b. p. 190°/0·5 mm., which after two crystallisations from ethanol formed yellow prisms (10 g., 23·6%), m. p. 92°. It was characterised by the *p-toluenesulphonamide*, colourless needles from alcohol, m. p. 106·5° (Found: C, 61·6; H, 4·8. $C_{20}H_{18}O_3NClS$ requires C, 61·9; H, 4·7%).

N-β-Diethylaminoethyl-3-chloro-4'-methoxydiphenylamine (II, R = $CH_2 \cdot CH_2 \cdot NEt_2$).—The magnesium salt prepared from methylmagnesium iodide and 3-chloro-4'-methoxydiphenylamine (10 g.) was alkylated with β-chloroethyldiethylamine (8·5 g.) in benzene (110 c.c.) and the product isolated as before. The fraction, b. p. 185—194°/0·2 mm. (4·5 g.,

31%), gave with saturated alcoholic oxalic acid the *oxalate* of *N*-β-diethylaminoethyl-3-chloro-4′-methoxydiphenylamine which crystallised from ethyl acetate in colourless needles, m. p. 139° (Found : C, 60·1; H, 6·4. $C_{19}H_{25}ON_2Cl,H_2C_2O_4$ requires C, 59·7; H, 6·4%). The amine *hydrochloride* was a microcrystalline powder, m. p. 159—160° (Found : Cl, 19·0. $C_{19}H_{25}ON_2Cl,HCl$ requires Cl, 19·3%).

N-β-*Diethylaminoethyl-4-methoxyphenyl-β-naphthylamine* (IV).—The greenish precipitate obtained on adding 4-methoxyphenyl-β-naphthylamine (10 g.) in dry xylene (120 c.c.) to ethereal methylmagnesium iodide in a hydrogen atmosphere was heated at 100° for 1½ hours with β-chloroethyldiethylamine (9·1 g.) and cuprous bromide (1·7 g.). Isolation in the usual way gave a base distilling at 210—215°/0·15 mm. as a pale orange viscous oil (4·1 g., 29%) easily oxidised in air, giving in ether solution a stable *hydrochloride* which crystallised from ethyl acetate–ether in colourless fine needles, m. p. 184·5° (Found : C, 71·6; H, 7·6. $C_{23}H_{28}ON_2,HCl$ requires C, 71·9; H, 7·6%).

2-*Nitro*-4-*methoxydiphenylamine*.—A mixture of 3-nitro-*p*-anisidine (50 g.), bromobenzene (270 c.c.) and potassium carbonate (21 g.) containing potassium iodide (1·5 g.) and freshly reduced copper (0·9 g.) (*Organic Syntheses*, 1936, **14**, 67) was heated under reflux in a metal-bath at 180°. Further quantities of the copper catalyst (1—2 g.) were added at intervals until the reaction was complete (16 hours); the product was filtered and the excess bromobenzene removed in steam. The residue was taken up in ether, and after washing with 2N hydrochloric acid the solution was evaporated. The product solidified on trituration with ligroin–alcohol, and recrystallisation from ether gave 2-*nitro*-4-*methoxydiphenylamine* (45·8 g., 62%) in shining red oblong plates, m. p. 48° (Found : C, 63·7; H, 4·8. $C_{13}H_{12}O_3N_2$ requires C, 63·9; H, 4·9%).

2-*Amino*-4-*methoxydiphenylamine* (V, R = H).—The nitro compound (38 g.) dissolved in alcohol (40 c.c.) was hydrogenated in the presence of Raney nickel under pressure at 50—60°. 2-*Amino*-4-*methoxydiphenylamine* separated on cooling, but owing to its speedy oxidation it was more conveniently purified by distillation; the pale yellow product (21 g., 63%), b. p. 155°/0·04 mm., had m. p. 98° (Found : C, 73·1; H, 6·7. $C_{13}H_{14}ON_2$ requires C, 72·9; H, 6·5%).

5-*Methoxy*-1-*phenyl*-2-*methylbenziminazole*.—After heating with β-chloroethyldiethylamine and sodium acetate in alcohol under pressure at 130—135° for 16 hours, 2-amino-4-methoxydiphenylamine was recovered unchanged. The aminodiphenylamine (5 g.) was then heated in nitrogen with sodamide (1·1 g.) and toluene (110 c.c.) at 100° (4 hours), and afterwards with acetyl chloride (2·4 g.). β-Chloroethyldiethylamine (32 g.) and sodamide (1·4 g.) were added and after 1 hour at room temperature, the mixture was heated at 100° for 4 hours and finally under reflux (½ hour). When this was cold, water was added and the toluene solution extracted with hydrochloric acid (0·02 N). The base, thus isolated, was refluxed with hydrochloric acid (12%), the solution made alkaline and extracted with ether to give a yellow oil, which distilled at 0·07 mm. (bath temp. 200°) and then solidified. Crystallisation from ligroin gave 5-*methoxy*-1-*phenyl*-2-*methylbenziminazole* (0·8 g.) as colourless slender needles, m. p. 103—105°, showing no tendency to discolour in air (Found : C, 75·4; H, 6·0. $C_{15}H_{14}ON_2$ requires C, 75·6; H, 5·9%).

2-p-*Toluenesulphon*-(γ-*diethylaminopropyl*)*amido*-4-*methoxydiphenylamine*.—A mixture of 2-amino-4-methoxydiphenylamine (5·7 g.), *p*-toluenesulphonyl chloride (5 g.) and pyridine heated at 100° for 3 hours and then digested with dilute acid, gave 2-p-*toluenesulphonamido*-4-*methoxydiphenylamine* (V, R = *p*-SO_2·C_6H_4·Me) (8·5 g.) crystallising from benzene–ligroin in pale pink stout prisms, m. p. 148° (Found : C, 65·3; H, 5·9; OMe, 7·7. $C_{20}H_{20}O_3N_2S$ requires C, 65·3; H, 5·4; OMe, 8·4%).

A solution of sodium (0·33 g.) in alcohol (17 c.c.) was treated with the sulphonamide (1·74 g.) and then with γ-chloropropyldiethylamine hydrochloride (1·76 g.). After refluxing for 2 hours, the filtered solution was evaporated and the residue crystallised from ligroin. The product (1·93 g., 84%), m. p. 84°, being inclined to oxidise, it was characterised as an *oxalate* which separated from alcohol–ether in long colourless prisms, m. p. 122° (Found : N, 7·2; S, 5·3. $C_{27}H_{35}O_3N_3S,C_2H_2O_4$ requires N, 7·3; S, 5·6%).

When dissolved in sulphuric acid (90%, 14 c.c.) and left at 0° for 18 hours, the aminosulphonamide (1·7 g.) was recovered unchanged. A solution of the compound (1·6 g.) in ether (20 c.c.) was dissolved in liquid ammonia to which sodium was added until a permanent blue colour appeared. Ammonium chloride was then used to remove excess sodium, and the ammonia allowed to evaporate. As this occurred, the product blackened in contact with the air. Attempts were made to isolate the amine by addition of water and precipitation of a hydrochloride from the dried ethereal extract, but the crystalline solid could not be obtained analytically pure.

N-β-*Diethylaminoethyl-αα-diphenylmethylamine*.—A solution of αα-diphenylmethylamine (44 g., 2 mol.) and β-chloroethyldiethylamine hydrochloride (24 g., *ca.* 1 mol.) in ethanol (50 c.c.) was heated in an autoclave at 110° for 6 hours. After evaporating the solvent and making alkaline, the product was collected in ether and distilled, the alkylated diphenylmethylamine, b. p. 200—210°/20 mm., giving a *dihydrochloride* (12 g., 23%) on treatment with concentrated hydrochloric acid. The salt crystallised from ethanol in colourless prisms, m. p. 244—245° (Found : C, 64·5; H, 7·7. $C_{19}H_{26}N_2,2HCl$ requires C, 64·2; H, 7·9%). The amine (b. p. 110—115°/0·1 mm.) was also obtained in approximately the same yield (27·5%) by alkylation of the magnesium derivative of αα-diphenylmethylamine prepared from methylmagnesium iodide (1 mol.) in the manner described for the chloromethoxy analogue below.

4-*Chloro*-3′-*aminobenzophenone*.—A solution of 4-chloro-3′-nitrobenzophenone (27 g., 1 mol.) in the minimum amount of ethanol was mixed with saturated alcoholic hydrogen chloride (350 c.c.). Hydrated stannous chloride (75 g., 3·5 mol.) was added at 0°, and after 1 hour, when solid had separated, the mixture was heated to 100° for 1 hour, and finally evaporated under diminished pressure. Treatment with concentrated sodium hydroxide solution liberated an oil which, after isolation with ether, solidified. 4-*Chloro*-3′-*aminobenzophenone* (23 g., 96%) crystallised from ethyl acetate–ligroin in pale yellow needles, m. p. 115° (Found : C, 67·4; H, 4·5. $C_{13}H_{10}ONCl$ requires C, 67·5; H, 4·3%).

4-*Chloro*-3′-*hydroxybenzophenone*.—A solution of the chloroaminobenzophenone (5 g.) in water (30 c.c.) and sulphuric acid (8 c.c.) treated below 0° with sodium nitrite (1·5 g.) in water (10 c.c.) gave the sparingly soluble diazonium salt. The suspension was slowly added to boiling copper sulphate solution, and the resulting brown solid taken up in ether. From the ethereal solution extraction with aqueous sodium hydroxide removed the crude 4-*chloro*-3′-*hydroxybenzophenone* (4·2 g., 84%), m. p. *ca.* 148°, which after 2 crystallisations from benzene formed colourless needles, m. p. 154—155° (Found : C, 67·3; H, 4·0. $C_{13}H_9O_2Cl$ requires C, 67·1; H, 3·9%).

4-*Chloro*-3′-*methoxybenzophenone*.—Methylation of the chlorohydroxybenzophenone with methyl sulphate in aqueous alkali gave poor yields, and two other methods were used. (i) A solution of the phenol (4 g.) in methanol (60 c.c.) containing sodium (0·8 g.) was treated with methyl sulphate (9 g.) and refluxed for 2 hours. The addition of ether and water, after evaporation of the solvent, gave an ethereal extract from which aqueous alkali removed unchanged hydroxyketone (1·3 g.) leaving the methoxy compound (1·65 g., 57·5%), b. p. 140—145°/0·01 mm. The *ketoxime*, crystallising in slender needles from aqueous alcohol, had m. p. 138° (Found : C, 64·4; H, 4·7. $C_{14}H_{12}O_2NCl$ requires C, 64·2; H, 4·6%). (ii) A methanol solution (50 c.c.) of the hydroxy compound (4 g.) was refluxed with methyl iodide (15 g.) and potassium carbonate (15 g.) for 10 hours and then filtered and evaporated. Isolation as in method (i) gave 4-chloro-3′-methoxybenzophenone as an oil (2·8 g., 66%) which solidified after distillation, crystallising from ligroin in prisms, m. p. 38°, and which was identified by the oxime, m. p. 138°.

4-*Chloro*-3′-*methoxy*-αα-*diphenylmethylamine* (III, R = H).—To ammonium formate which had been heated at 165° for 1 hour, 4-chloro-3′-methoxybenzophenone (5·4 g.) was added, and the mixture heated at 180—190° for 4 hours The

viscous product was heated under reflux for an hour with water (60 c.c.) and concentrated hydrochloric acid (150 c.c.), and on cooling the diphenylmethylamine hydrochloride (4·5 g., 72·5%) separated. Crystallised from ethanol–*cyclo*hexane, it had m. p. 175°, and gave with alkali the free base, of which the *picrate* crystallised from *cyclo*hexane in fine yellow needles, m. p. 199° (Found: C, 50·5; H, 3·8. $C_{14}H_{14}ONCl,C_6H_3O_7N_3$ requires C, 50·4; H, 3·6%).

N-β-Diethylaminoethyl-4-chloro-3′-methoxy-αα-diphenylmethylamine (III, R = $CH_2{\cdot}CH_2{\cdot}NEt_2$).—A solution of the Grignard reagent prepared from magnesium (0·29 g., 1 mol.) and methyl iodide (1·7 g.) in ether (120 c.c.), and containing 4-chloro-3′-methoxydiphenylmethylamine (3 g., 1 mol.) after standing for 3 hours was heated to boiling for ½ hour. Heating was continued for 2 hours with β-chloroethyldiethylamine (1·6 g., 1 mol.) and cuprous bromide (0·5 g.) and, after evaporation of the solvent, for 2 hours at 100°. The product was isolated by adding saturated aqueous ammonium chloride and dissolving the brown gummy solid in benzene, from which hydrochloric acid (15%) extracted the required amine. When precipitated with alkali and distilled, *N-β*-diethylaminoethyl-4-chloro-3′-methoxy-αα-diphenylmethylamine was a pale yellow syrup (1·92 g., 47%) giving a crystalline but highly deliquescent hydrochloride. Accordingly the *dipicrate* which crystallised from ethyl acetate in fine yellow needles, m. p. 182°, was prepared for analysis (Found: C, 48·0; H, 4·0. $C_{29}H_{27}ON_9Cl,2C_6H_3O_7N_3$ requires C, 47·7; H, 4·1%).

4-Chloro-4′-methoxy-αα-diphenylmethylamine.—The product obtained by heating 4-chloro-4′-methoxybenzophenone (23 g.) (Peterson, *loc. cit.*) with ammonium formate (33 g.) as described in the preparation of (III, R = H) was hydrolysed by boiling with hydrochloric acid (320 c.c. of 27%) for 1 hour. The amine *hydrochloride*, which separated in the cold, crystallised from hydrochloric acid in colourless needles (20 g., 87%), m. p. 234—235° (Found: C, 58·9; H, 5·3. $C_{14}H_{14}ONCl,HCl$ requires C, 59·2; H, 5·3%).

N-β-Diethylaminoethyl-4-chloro-4′-methoxy-αα-diphenylmethylamine.—The hydrochlorides of the foregoing diphenylmethylamine (5 g.) and of β-chloroethyldiethylamine (4·5 g.) were heated with fused sodium acetate (3·6 g.) in ethanol (25 c.c.) in a sealed tube for 17 hours at 120°. The base (2·7 g., 44%) isolated by distillation of the filtered solution had b. p. 175—180°/0·05 mm., and gave a *hydrochloride* crystallising from ethanol–ether in colourless tablets (1·6 g., 21%), m. p. 183° (Found: C, 54·8; H, 7·1; N, 7·0. $C_{29}H_{27}ON_9Cl,2HCl,H_2O$ requires C, 54·8; H, 7·1; N, 6·4%. Found after drying to constant weight: loss, 3·3; Cl, 25·0. $C_{29}H_{27}ON_9Cl,2HCl$ requires H_2O, 4·1; Cl, 25·4%).

N-γ-Diethylaminopropyl-4-chloro-4′-methoxy-αα-diphenylmethylamine.—Under the conditions of the preceding experiment, 4-chloro-4′-methoxydiphenylmethylamine reacted with γ-chloropropyldiethylamine to give the *N-γ*-diethylaminopropyl derivative (yield 79%), as a partly crystalline viscous mass, b. p. 180—185°/0·07 mm., characterised by a *dioxalate* crystallising from ethanol–ether in colourless needles, m. p. 142—145° (Found: C, 55·5; H, 6·4; N, 4·7. $C_{21}H_{29}ON_3Cl,2H_2C_2O_4$ requires C, 55·5; H, 6·1; N, 5·2%). The hydrochloride of the base obtained from the purified oxalate was an uncrystallisable syrup.

Methyl α-Hydroxy-α-m-methoxyphenylacetiminate.—*m*-Methoxybenzaldehyde (40 g.) was converted into the cyanohydrin by the standard method (cf. *Organic Syntheses*, 1926, **6**, 58), and its ethereal solution (*ca.* 200 c.c.) dried over potassium carbonate. Absolute methanol (7 g.) and dry hydrogen chloride (21 g.) were then added at −5°, and after 24 hours the crystalline *hydrochloride* (36 g.) was collected. The salt separated in colourless long thin prisms, m. p. 105° (efferv.) (Found: C, 51·8; H, 6·3; N, 6·1. $C_{10}H_{13}O_2N,HCl$ requires C, 51·8; H, 6·1; N, 6·1%).

α-Hydroxy-α-m-methoxyphenylacetamidine.—The imino-ester hydrochloride (36 g.) was added to a solution of anhydrous ammonia (25 g.) in methanol at −5° and left overnight. Concentrating the filtered liquid under reduced pressure to 75 c.c. and treating with ethyl acetate (150 c.c.) precipitated the amidine *hydrochloride* (27 g., 80%) which after recrystallisation from ethanol–ether formed colourless plates, m. p. 190° (Found: N, 13·1. $C_9H_{12}O_2N_2,HCl$ requires N, 12·9%).

4-Hydroxy-2-(α-hydroxy-m-methoxybenzyl)-6-methylpyrimidine (VI, R = OH).—The amidine hydrochloride (30 g.) and ethyl acetoacetate (18·2 g.) were dissolved in a solution of sodium hydroxide (11·2 g.) in water (20 c.c.) and ethanol (100 c.c.), and left at room temperature for 24 hours. Water (400 c.c.) was then added, the solution filtered and made slightly acid with hydrochloric acid. The precipitated solid (23 g., 68%) was collected and crystallised from water, from which it separated in colourless long thin prisms, m. p. 207°, very sparingly soluble in cold water and organic solvents (Found: C, 63·3; H, 5·8. $C_{13}H_{14}O_3N_2$ requires C, 63·4; H, 5·7%).

2-(α-Chloro-m-methoxybenzyl)-4-hydroxy-6-methylpyrimidine (VI, R = Cl).—A suspension of the pyrimidine (VI, R = OH) (17 g.) in chloroform (50 c.c.) at −10° was treated with thionyl chloride added in 15 minutes and then left at 0° for 12 hours. Evaporation of the clear solution yielded a pale yellow gum which gave a colourless solid (14·7 g., 81%). When recrystallised from a small volume of ethanol the *chloropyrimidine* was obtained as needles, m. p. 159—160° (Found: C, 58·9; H, 5·2; Cl, 13·0. $C_{13}H_{13}O_2N_2Cl$ requires C, 59·0; H, 4·9; Cl, 13·4%).

4-Hydroxy-2-[α-(γ-diethylaminopropyl)amino-m-methoxybenzyl]-6-methylpyrimidine (VI, R = $NH{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}NEt_2$).—The chloropyrimidine (VI, R = Cl) (5·8 g., 1 mol.) and γ-diethylaminopropylamine (5·7 g., 2 mol.) were heated in refluxing ethanol (50 c.c.) for 9 hours. The solvent was then evaporated, the residue treated with excess aqueous sodium carbonate and extracted with chloroform. The chloroform solution was shaken 3 times with aqueous sodium hydroxide (0·5N), the combined extracts strongly acidified, and unchanged chloropyrimidine (1·7 g.) removed by chloroform. The aqueous acid solution was then made alkaline with sodium carbonate and the liberated amine taken up in chloroform. Evaporation gave a dark amber gum (3·5 g., 64%) which yielded deliquescent products with hydrogen chloride and oxalic acid, but a crystalline *dipicrate* separated on mixing methanolic solutions of the base and picric acid. It crystallised from acetone–ether in minute yellow tablets, m. p. 170—171° (Found: C, 46·9; H, 4·8. $C_{20}H_{30}O_2N_4,2C_6H_3O_7N_3$ requires C, 47·1; H, 4·4). The sparingly soluble *dipicrolonate*, prepared in methanol–acetone and crystallised from *cyclo*hexanone–ether, consisted of minute needles, m. p. 215° (decomp.) (Found: C, 53·1; H, 5·2; N, 18·5. $C_{20}H_{30}O_2N_4,2C_{10}H_8O_5N_4,H_2O$ requires C, 53·3: H, 5·3; N, 19·0%).

α-Hydroxy-α-o-chlorophenylacetamidine.—The crude cyanohydrin of *o*-chlorobenzaldehyde (70 g.) dissolved in ether containing methanol and hydrogen chloride very rapidly deposited *methyl α-hydroxy-α-o-chlorophenylacetiminate hydrochloride* (88 g.) in colourless needles, m. p. 128° (Found: 45·7; H, 4·6. $C_9H_{10}O_2NCl,HCl$ requires C, 45·8; H, 4·7%). Alcoholic ammonia converted the salt into the amidine *hydrochloride* crystallising from ethanol–ethyl acetate in microscopic plates, m. p. 171° (Found: C, 43·1; H, 4·7. $C_8H_{10}ON_2Cl_2$ requires C, 43·4; H, 4·5%).

4-Hydroxy-2-(α-chloro-o-chlorobenzyl)-6-methylpyrimidine.—Condensation of the *o*-chlorophenacetamidine with ethyl acetoacetate in aqueous alcoholic alkali gave *4-hydroxy-2-(α-hydroxy-o-chlorobenzyl)-6-methylpyrimidine* (69%) which separated from water in colourless cubes, m. p. 195—196° (Found: C, 57·5; H, 4·5; N, 11·1. $C_{13}H_{11}O_2N_2Cl$ requires C, 57·5; H, 4·4; N, 11·2%). As with the pyrimidine (VI, R = OH), cold thionyl chloride gave the chloropyrimidine (97%), and the pure product crystallised from aqueous alcohol in long prisms, m. p. 197° (Found: C, 53·7; H, 3·9. $C_{12}H_{10}ON_2Cl_2$ requires C, 53·6; H, 3·7%).

4-Hydroxy-2-[α-(γ-diethylaminopropyl)amino-o-chlorobenzyl]-6-methylpyrimidine.—Alkylation of the foregoing pyrimidine with γ-diethylaminopropylamine was effected exactly as with its *m*-methoxy analogue, and gave a 65% yield of the crude amine. The salts of this product, *e.g.*, hydrochloride, sulphate, oxalate, picrate, styphnate, trinitrobenzoate and meconate, showed great reluctance to crystallise. Eventually the amine was characterised by a *dipicrolonate* crystallising from ethanol–ether in pale yellow leaflets, m. p. 197° (decomp.) (Found: C, 52·1; H, 5·0; Cl, 4·1. $C_{19}H_{27}ON_4Cl,2C_{10}H_8O_5N_4$ requires C, 52·5; H, 4·8; Cl, 4·0%). By decomposition of the purified picrolonate with hydro-

chloric acid the *trihydrochloride* was obtained. The product, a straw-coloured gum, was analysed after several precipitations from methanol–ethyl acetate (Found: C, 48·7; H, 6·4; N, 11·8. $C_{19}H_{27}ON_4Cl,3HCl$ requires C, 48·3; H, 6·4; N, 11·9%).

The diethylaminoalkylamino-quinoxalines and -benzcinnolines of Parts I and II (*J.*, 1945, 791, 824) also have been tested against *P. gallinaceum* infections in chicks, and with the exception of (V, R = $-CH_2{\cdot}CH_2{\cdot}NEt_2$) of Part I, against *P. relictum* in canaries. It is now possible to state that all are devoid of antimalarial activity.

This investigation was carried out for the Chemotherapy Committee of the Medical Research Council to which two of us (T. J. K. and I. H. M. M.) are indebted for grants. We also thank Miss A. Bishop, Molteno Institute, Cambridge, and Miss I. M. Tonkin, National Institute for Medical Research, London, for the biological tests, and Mr. R. M. Acheson, for assistance with some of the synthetical work.

DYSON PERRINS LABORATORY, OXFORD. [*Received, October 8th*, 1945.]

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3. *The Course of Autoxidation Reactions in Polyisoprenes and Allied Compounds. Part XI. Double Bond Movement during the Autoxidation of a Mono-olefin.*

By E. HAROLD FARMER and DONALD A. SUTTON.

The peroxidation product obtained by photo-oxidation of 1 : 2-dimethyl-Δ^1-*cyclo*hexene appears to contain both 1 : 2-dimethyl-Δ^1-*cyclo*hexene-3-hydroperoxide and 1 : 2-dimethyl-Δ^2-*cyclo*hexene-1-hydroperoxide in accordance with the radical hydroperoxidation hypothesis previously advanced (Part VII), since its hydrogenation product contains about equal amounts of the corresponding saturated secondary and tertiary alcohols. The crystalline acidic by-product obtained by the action of alkali on the hydroperoxidation product of either 1-methyl-Δ^1-*cyclo*hexene or 1 : 2-dimethyl-Δ^1-*cyclo*hexene is the dihydroresorcinol, 2-methyl*cyclo*hexan-1 : 3-dione.

IN Part VII (Farmer, Koch, and Sutton, *J.*, 1943, 541) it was shown that the autoxidation of $\Delta^{1:4}$-dienes and $\Delta^{1:4:7}$-, etc., polyene compounds produces peroxido-derivatives containing conjugated units, and to explain the formation of the latter a reaction-mechanism was proposed which postulated the detachment of hydrogen *atoms* from the reactive methylene groups under the action of molecular oxygen, and subsequent re-arrangement of the resonating radical residues before oxygen and, finally, hydrogen combine therewith to give hydroperoxides:

$$\cdot CH{:}CH{\cdot}CH_2{\cdot}CH{:}CH{\cdot}CH_2{\cdot}CH{:}CH\cdot \longrightarrow \cdot CH{:}CH{\cdot}\overset{*}{C}H{\cdot}CH{:}CH{\cdot}CH_2{\cdot}CH{:}CH\cdot \rightleftharpoons$$

$$\cdot\overset{*}{C}H{\cdot}CH{:}CH{\cdot}CH{:}CH{\cdot}CH_2{\cdot}CH{:}CH\cdot \text{ or } \cdot CH{:}CH{\cdot}CH{:}CH{\cdot}\overset{*}{C}H{\cdot}CH_2{\cdot}CH{:}CH\cdot \xrightarrow{O_2} \text{Hydroperoxides}$$

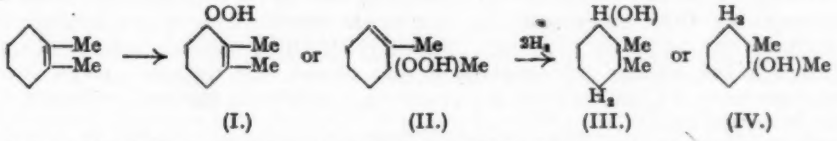
It was recognised that, if this mechanism is valid for methylene-interrupted diene- or polyene-systems, it might reasonably be expected to apply also to the formation of hydroperoxides by the action of oxygen either on simple olefins or on polyolefins containing two or more methylene groups between the double bonds. In order to demonstrate successfully that even the simplest olefin system capable of hydroperoxidation can give both of the oxygenated forms (A) and (B),

$$\cdot CH_2{\cdot}CH{:}CH\cdot \xrightarrow{-H} \cdot CH{\cdots}CH{\cdots}CH\cdot \xrightarrow[H]{O_2} \underset{\text{(A.)}}{\cdot CH(OOH){\cdot}CH{:}CH\cdot} \text{ and } \underset{\text{(B.)}}{\cdot CH{:}CH{\cdot}CH(OOH)\cdot},$$

it is necessary for practical reasons to fulfil three conditions, viz., (*a*) the hydroperoxide(s) formed by autoxidation must be sufficiently stable to survive in good yield until the required amount of oxygen has been absorbed, (*b*) the olefin selected must be of such convenient constitution that the task of distinguishing structurally between the expected isomeric hydroperoxides is not unduly difficult, and (*c*) the hydroperoxides formed must be capable of transformation into identifiable derivatives without undergoing too high a proportion of secondary change (*i.e.*, change involving isomerisation by oxygen-redistribution or oxidative degradation). Various of the simple olefinic substances so far used in our autoxidation experiments, and especially the *cyclo*hexenes as a group, satisfy the first condition, some few are able to satisfy the second, but few are found in practice to satisfy the third. For a first attempt, to demonstrate the occurrence of double bond shift during hydroperoxidation, 1 : 2-dimethyl-Δ^1-*cyclo*hexene seemed most suitable, for, although the degree of its satisfaction of the third condition left a good deal to be desired—at any rate in respect of identification by hydrogenation—it successfully complied with the second in that its two alkyl groups could serve as reference points for recognising double bond shift if it occurred, and also by their presence could prevent unwanted isomerism arising from hydroperoxidation at alternative methylene groups in the system $\cdot CH_2{\cdot}CH{:}CH{\cdot}CH_2$.

The formation and rectification of the hydroperoxide of 1 : 2-dimethyl-Δ^1-*cyclo*hexene has already been described by Farmer and Sundralingam (*J.*, 1942, 121). An unexpected feature of the freshly distilled peroxide was that the peroxide-content ($\cdot O{\cdot}O\cdot$) as measured by the colorimetric method of Bolland *et al.* (*Trans. Inst. Rubber Ind.*, 1941, **16**, 29), which has usually been found to be very dependable for this type of peroxide, was considerably higher than the theoretical, but as measured by the potassium iodide method of Dastur and Lea (*Analyst*, 1941, **66**, 90) was considerably lower than the theoretical. When the peroxide had been kept for 5 days at 0° the colorimetric value fell to near the theoretical, while the content as measured by the potassium iodide method fell somewhat also. The causes controlling the appearance of this phenomenon are not understood at present, but as the phenomenon has now been observed in connection with several other olefinic

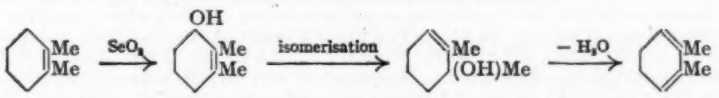
peroxides it apparently means that some of the molecules of certain freshly distilled peroxides are able to use both of their oxygen atoms for the oxidation of ferrous sulphate and not only one as is normally the case.* By use of a mixed platinum-palladium catalyst which is usually more successful than platinum alone for peroxide reductions (cf. Bodendorf, *Arch. Pharm.*, **1933**, **271**, 1) the hydrogenation of the peroxide in the normal fashion could only be effected to the extent of *ca.* 75%, and the product of this reaction was a mixture of alcohols having the required composition $C_8H_{15}(OH)$. This mixture proved to consist of approximately equal amounts of the secondary alcohol (III) (isolated and identified), and of the tertiary isomer (IV), the presence of which was indicated by the production of 1 : 2-dimethyl-Δ^1-*cyclo*hexene on dehydration by heat in the presence of traces of iodine.



(I.) (II.) (III.) (IV.)

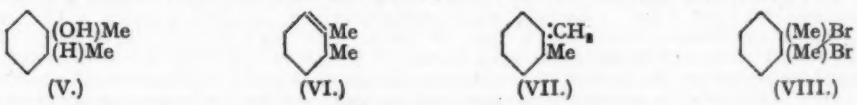
Thus, it may be inferred that the two hydroperoxides (I) and (II), *i.e.*, the structures which are to be expected in terms of the radical hydroperoxidation hypothesis, were both present in the oxidation product, and hence that the autoxidation of simple olefins can actually be accompanied by a considerable degree of double bond shift.

This demonstration of course depends for its validity on the absence of anionotropic interchange between the alcohols (III) and (IV), or between the formed hydroperoxide molecules (I) and (II), but since (i) the existing evidence relating to the mechanism of peroxidation (especially photo-oxidation as here used) is overwhelmingly in favour of a radical chain-process, and (ii) the experimental conditions of peroxidation and hydrogenation were not such as would promote the separation of anions, the occurrence of any significant degree of anionotropy seems unlikely. In the comparable case of the oxidation of 1 : 2-dimethyl-Δ^1-*cyclo*hexene by selenium dioxide, the product from which was shown by Guillemonat (*Ann. Chim.*, 1939, **11**, 141) to contain the conjugated diene 1 : 2-dimethyl-$\Delta^{2:6}$-*cyclo*hexadiene, formed in his view by the following steps :



the absence of anionotropy is perhaps less certain, since the selenium oxide was used in conjunction with acetic acid–acetic anhydride. If, however, oxidation by selenium dioxide, like peroxidation, involves a radical mechanism, the secondary alcohol represented above as the precursor of the diene might well be a primary product of reaction.

It should be mentioned that dimethyl*cyclo*hexene prepared by distillation of the tertiary alcohol (V) in presence of a little iodine, which has been assumed by successive workers to be the pure 1 : 2-dimethyl-Δ^1-



(V.) (VI.) (VII.) (VIII.)

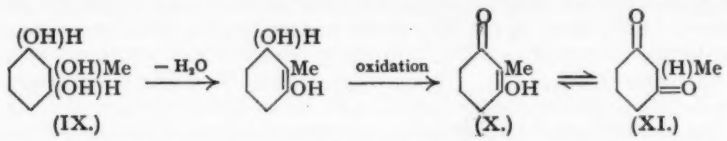
*cyclo*hexene, could conceivably contain substantial amounts of the isomeric Δ^2 compound (VI) as also a little of the isomeric methylene compound (VII) and, indeed, Lebedev *et al.* (*J.*, 1925, 417; 1930, 321) have claimed that rate-of-hydrogenation tests show that the dimethyl*cyclo*hexene formed by a variant process, viz., the dehydration of (V) with 30% sulphuric acid, is actually a mixture of all three isomeric olefins. The foregoing demonstration was carried out in the first place with carefully rectified dimethyl*cyclo*hexene prepared by the iodine-dehydration method, which at no stage gave indication of containing any significant amount of (VI) or (VII), the former of which by its presence must have invalidated the work. To remove all uncertainty, the demonstration was repeated with a sample of homogeneous dimethyl*cyclo*hexene regenerated from the crystalline dibromide (VIII) (which incidentally agreed exactly in physical constants with the iodine-dehydration product) without any important difference accruing in the result.

The opportunity presented by the present investigation has been taken to identify the only secondary derivative of *cyclo*hexene autoxidation products so far isolated which remained uncorrelated with the general hydroperoxidation scheme developed in previous papers of the series. The compound in question was the crystalline acidic by-product, $C_7H_{10}O_3$, formed by the action of aqueous alkali on (apparently)† either 1-methyl-*cyclo*hexene-3-hydroperoxide or 1 : 2-dimethyl*cyclo*hexene-3-hydroperoxide. The compound, from the mono-methyl-hydroperoxide, was re-prepared and found to exhibit a characteristic absorption spectrum, that of 2-methyl*cyclo*hexan-1 : 3-dione. This, together with its mono-acidity, its crystalline nature, and easy oxidisability by permanganate (cf., Farmer and Sundralingam, *loc. cit.*, pp. 136, 137) to give an acid, identified as

* The peroxide content is by definition twice the active oxygen content as measured experimentally, so that if more than one atomic proportion of oxygen from each ·OO· grouping becomes available as active oxygen, the peroxide value found experimentally may considerably exceed the total oxygen content in the compound as determined by elementary analysis. This apparent absurdity is encountered in the present case.

† The formation from either has now been shown with certainty.

glutaric acid, leaves no doubt as to its being the methyldihydroresorcinol (X, XI). The formation of the latter cannot easily be accounted for except on the basis of dehydration of the triol (IX) (a major product of the



(IX.) (X.) (XI.)

treatment with alkali), followed by oxidation of the resulting enol to the corresponding dione by active oxygen derived from decomposing ·OOH groups. In the case of the dimethyl*cyclo*hexene hydroperoxide, the corresponding triol contains the pinacolic grouping, ·CMe(OH)·CMe(OH)·, which is able to liberate both methyl and hydroxyl groups in the manner characteristic of pinacolones. Of the two possible courses of reaction, viz., to give the pinacolone, R·CMe·CO·R′, or (by elimination of MeOH) the enol, ·CMe:C(OH)·, the latter is found in practice to be preferred.

Experimental.

1 : 2-*Dimethyl*cyclo*hexene Hydroperoxide.*—1 : 2-Dimethyl*cyclo*hexene (75 g.), prepared by the dehydration of 1 : 2-dimethyl*cyclo*hexan-1-ol in the presence of iodine (Signaigo and Cramer, *J. Amer. Chem. Soc.*, 1933, **55**, 3326), was oxidised at 35° in a quartz flask illuminated by a Hanovia U.V.S. 500 lamp. During 210 minutes oxygen (6 litres) was absorbed. After removal of unchanged hydrocarbon (*ca.* 30 g.) and other easily volatile products by gentle heating (bath below 45°) the residue was fractionally distilled at <1 mm. The main peroxide fraction (12·2 g.), distilling at 70—75°/0·5 mm., had $n_D^{15°}$ 1·4908 (Found : C, 68·75; H, 10·1. Calc. for $C_8H_{14}O_2$: C, 67·55, H, 9·9%). It was a colourless oil which (when determined immediately for peroxide by the colorimetric method of Bolland *et al.*, *loc. cit.*), gave P.O.C. 28·4% (calc. for pure peroxide : P.O.C., 22·2%), but after being kept for 5 days at 0° gave P.O.C. 21·4% by the colorimetric method but only 14·4% by the potassium iodide method of Dastur and Lea (*loc. cit.*). On refractionation, the main distillate (b. p. 72—74°/0·5 mm.; 11·5 g.) then had C, 69·15; H, 10·15; P.O.C. (colorimetric) 29·7; P.O.C. (potassium iodide method) 17·7%.

Hydrogenation of the Hydroperoxide.—The re-fractionated hydroperoxide (10·8 g.) was dissolved in absolute alcohol (100 c.c.) and hydrogenated in the presence of 0·4 g. of freshly prepared Adams's platinum catalyst. Rapid absorption of 1470 c.c. (N.T.P.) of hydrogen occurred, but then no more gas was taken up even after a further 0·4 g. of catalyst had been added and the reaction mixture warmed to 55°. The filtered mixture was distilled; the main (alcoholic) oxidation product (7·2 g.) had b. p. 52°/0·1 mm., $n_D^{16°}$ 1·4790 (Found : C, 74·9; H, 11·6. Calc. for $C_8H_{16}O$: C, 75·0; H, 12·5%), and was, therefore, incompletely saturated. This product was dissolved in pure ethanol (125 c.c.) and shaken in hydrogen at 65° with a mixture of 0·4 g. each of Adams's platinum and palladium catalysts. A further slow uptake of hydrogen set in, and continued until saturation was substantially complete. The distilled reduction product consisted mainly of an alcoholic product (5·7 g.) having b. p. 50—54°/0·1 mm., $n_D^{20°}$ 1·4647 (Found : C, 73·75; H, 12·35%).

Composition of Hydrogenation Product.—The almost saturated reduction product (3·4 g.) was heated with a few small crystals of iodine at 180—190° for 30 minutes and the dehydrated material allowed to distil. The oily distillate (1·8 g.) was well washed with water, dried over calcium chloride and distilled over sodium. The product was a slightly impure hydrocarbon (1·1 g.) having $n_D^{17°}$ 1·4598 (Found : C, 85·6; H, 12·7. Calc. for C_8H_{14} : C, 87·2; H, 12·8%). This was converted into the corresponding bromo-adduct by dissolving it in pure chloroform (2 c.c.) and adding to the solution at 0° bromine (1·8 g.) dissolved in chloroform (2 c.c.). The adduct, when worked up, consisted of a mixture of oily and crystalline dibromides; the solid (1·0 g.), after being twice crystallised from dry alcohol, had m. p. 151° and was identified as pure 1 : 2-dimethyl-Δ^1-*cyclo*hexene dibromide (Found : Br, 59·35. Calc. for $C_8H_{14}Br_2$: Br, 59·35%). Repetition of the bromination using pure 1 : 2-dimethyl*cyclo*hexene gave an exactly similar result, 1·2 g. of the dibromide being obtained. Thus, the hydrocarbon formed by the dehydration consisted almost wholly of 1 : 2-dimethyl-Δ^1-*cyclo*hexene.

The portion of the hydrogenation product which remained undehydrated by the iodine-treatment gave on distillation an alcohol (0·9 g.) having b. p. 68—72°/12 mm. This alcohol, crude 1 : 2-dimethyl*cyclo*hexan-3-ol, gave, when heated at 110—120° for 30 minutes with α-naphthyl *iso*cyanate (1·3 g.), a crude *urethane* (0·6 g), m. p. 134—137°, which, after recrystallisation from ligroin (b. p. 100—120°), formed colourless prisms, m. p. 141° (Found : C, 76·55; H, 7·6; N, 4·75. $C_{19}H_{23}O_2N$ requires : C, 76·75; H, 7·8; N, 4·7%). The same α-naphthyl urethane (m. p. 140°) could also be formed, although in poor yield, from the unfractionated hydrogenation product (Found : C, 76·75; H, 8·0; N, 4·7%); the diminished yield is probably due to some dehydration of the tertiary alcohol by the *iso*cyanate, since Bickel and French (*J. Amer. Chem. Soc.*, 1926, **48**, 747) have observed that free water has an adverse effect on the reaction of α-naphthyl *iso*cyanate with secondary alcohols. The urethane showed no depression of melting point when mixed with an authentic specimen (below).

Synthesis of 1 : 2-*Dimethyl*cyclo*hexan*-3-*ol.*—*o*-Xylene (200 g.) was nitrated by the method of Emerson and Smith (*loc. cit.*) and converted into 3-nitro-*o*-xylene (118 g.). The latter was converted *via* the corresponding amine (85 g.) and then the iodide (124 g.) into crude 2 : 3-dimethylphenol (56 g.). The crude phenol melted at 44—47° (Smith and Opie record m. p. 65—66°), but, after several crystallisations from ligroin (b. p. 40—60°) a fraction was isolated having m. p. 71—73° (Short, Stromberg and Wiles, *J.*, 1936, 322, record 73·5—74·5°; Kruber and Schmidt, *Ber.*, 1931, **64**, 2274, record 75°); the residue doubtless contained isomers of the desired 2 : 3-dimethylphenol, formed by nitration occurring elsewhere than at the 3-position. Hydrogenation of the compound, m. p. 71—73°, was conducted in ethanol (100 c.c.) at 180°/100 atm., using Raney nickel as catalyst, this procedure being more satisfactory than that employed by Sabatier and Mailhe (*Compt. rend.*, 1906, **142**, 553) for 3 : 4-dimethylphenol. The hydrogenation gave a product from which 1 : 2-*dimethyl*cyclo*hexan*-3-*ol* (13 g.) was isolated by fractional distillation; this had b. p. 77—79°/12 mm. and $n_D^{18°}$ 1·4662 (Found : C, 74·65; H, 12·55. $C_8H_{16}O$ requires C, 75·0; H, 12·5%). The synthetic alcohol (1 g.) gave when heated with α-naphthyl *iso*cyanate (1 g.) at 110—120° for 30 minutes the corresponding urethane, m. p. 130—133° (0·6 g.) which on recrystallisation melted at 138—140° (Found : C, 76·65; H, 7·8; N, 4·60%).

Decomposition of 1-*Methyl*-Δ^1-cyclo*hexene*-5-*hydroperoxide with Alkali.*—1- Methyl*cyclo*hexene hydroperoxide (12·5 g.), prepared as described by Farmer and Sundralingam (*loc. cit.*), was mechanically shaken with 300 c.c. of N sodium hydroxide. The aqueous product was thoroughly extracted with ether, then acidified with 6N sulphuric acid, and finally continuously extracted with ether for 7 hours. The dried ether extract gave, on evaporation, an oily liquid containing some suspended crystals, m. p. 196—199°. The latter, recrystallised from 96% alcohol, had m. p. 205—207° (0·2 g.) (Found : C, 66·75; H, 8·2. Calc. for $C_7H_{10}O_2$: C, 66·65; H, 8·0%), the same as that recorded by Butz (*J. Org. Chem.*, 1943, **8**, 515) for 2-methyl*cyclo*hexan-1 : 3-dione. The absorption spectrum of this material, kindly determined for us by Dr. H. P. Koch,

had the characteristics: Max. A., 2620; Σ, 17,000 (0·001 molar solution used). Butz (*loc. cit.*) records for methyl*cyclo*hexandione: max. 2610 A.,; Σ, 17,000 (0·000606 molar solution used).

Purification of 1 : 2-*Dimethyl*-Δ^1-cyclo*hexene*.—The hydrocarbon, prepared as described above by dehydration of 1 : 2-dimethyl*cyclo*hexan-1-ol in presence of a little iodine (95 g.), was dissolved in chloroform (150 c.c.) and treated, while cooled in ice–salt, with bromine (138 g.) dissolved in chloroform (150 c.c.) during 3½ hours with rapid stirring. The solvent was removed under reduced pressure (below 50°) and the residual mixture of solid and liquid dibromides filtered. The liquid dibromide was not used, but the solid was collected and crystallised several times from dry ethanol, the dissolution on each occasion being conducted with the minimum of heating (owing to the ready interaction of the bromide and alcohol to form ethoxy compounds) and the crystallisation each time rapidly promoted by rapidly cooling the solution to −5°. At best, only 85 g. of solid dibromide having m. p. 145—148° together with 17 g. of somewhat impure dibromide (m. p. 140—145°) survived this extremely wasteful crystallisation.

The hydrocarbon was regenerated from the pure solid dibromide (97 g.) by dissolving the latter in pure acetone containing a trace of zinc chloride and debrominating it with zinc. For this purpose, the solution, contained in a flask provided with a gas inlet tube and a reflux condenser, was treated with granulated zinc (50 g.) in portions, the reaction mixture being warmed at the beginning to promote reaction. When ebullition had ceased the reaction product was cooled, poured into water and the oily hydrocarbon taken up in ether. The ether extract was dried over potassium carbonate and the ether removed through a column; the residual dimethyl*cyclo*hexene was twice distilled over sodium in an atmosphere of pure nitrogen, and the product (14·0 g.) had b. p. 134°, and $n_D^{15°}$ 1·4616 (Found: C, 87·1; H, 12·8. Calc. for C_8H_{14}: C, 87·2; H, 12·8%). Dimethyl*cyclo*hexene, ordinarily obtained by the iodine dehydration method, has n_D^{15} 1·4610.

Peroxidation of Pure 1 : 2-*Dimethyl*-Δ^1-cyclo*hexene*.—The pure hydrocarbon obtained by debromination of solid dimethyl*cyclo*hexene dibromide was oxidised in U.V. light and the oxidation product rectified and finally hydrogenated all exactly as described above. The behaviour throughout, and the products of peroxidation and of hydrogenation, agreed so closely with those described above for "ordinary" dimethyl*cyclo*hexene, that further description is unnecessary. Clearly, both a primary and a tertiary dimethyl*cyclo*hexene can be obtained by hydrogenation of the hydroperoxidation product of homogeneous 1 : 2-dimethyl*cyclo*hexene.

This work forms part of a programme of fundamental investigation on rubber undertaken by the Board of the British Rubber Producers' Research Association.

BRITISH RUBBER PRODUCERS' RESEARCH ASSOCIATION,
48, TEWIN ROAD, WELWYN GARDEN CITY, HERTS.

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4. *The Acetone Derivatives of Hexahydric Alcohols. Part I. Triacetone Mannitol and its Conversion into* d-*Arabinose.*

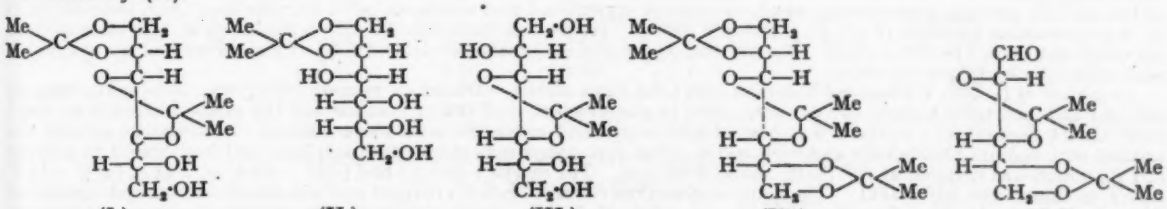
By L. F. WIGGINS.

Evidence is presented for the structure of fully acetonised mannitol as 1 : 2-3 : 4-5 : 6-triacetone mannitol. Its graded hydrolysis yields 3 : 4-monoacetone mannitol and also 1 : 2-3 : 4-diacetone mannitol which is converted through oxidation with lead tetra-acetate into diacetone aldehydo-*d*-arabinose and thence into *d*-arabinose.

TRIACETONE mannitol was first prepared by Fischer (*Ber.*, 1895, **28**, 1167) but it was not until 1914 that a constitution was suggested. Irvine and Patterson (*J.*, 1914, **105**, 898) carried out a graded hydrolysis of triacetone mannitol, and isolated a diacetone and a monoacetone mannitol, the former being designated as the α-form since it was different from the β-diacetone mannitol which Fischer (*loc. cit.*) isolated as a by-product in the acetonisation of mannitol and which was later shown to be 1 : 2-5 : 6-diacetone mannitol (Baer and H. O. L. Fischer, *Helv. Chim. Acta*, 1934, **17**, 622; *J. Biol. Chem.*, 1939, **128**, 463).

Although Irvine and Patterson's structure for triacetone mannitol is now shown to be correct, it was based on no very firm ground. Later workers have sought to correct parts of this earlier work, but the whole position needs clarification and this is attempted in the following argument.

Irvine and Patterson (*loc. cit.*) considered α-diacetone mannitol to be represented by (I) and monoacetone mannitol by (II).



(I.) (II.) (III.) (IV.) (V.)

The structure (I) was based on the oxidation of the dimethyl mannitol, obtained by methylation and subsequent hydrolysis of diacetone mannitol, to dimethyl mannonolactone which appeared to be a γ-lactone, although the attachment of the methyl groups at C_5 and C_6 was not rigorously proved. Formula (II) was based on the oxidation of the partly methylated mannitol, obtained by methylation followed by hydrolysis of monoacetone mannitol, to a so-called tetramethyl mannonic acid which would not lactonise. The structure (II) for monoacetone mannitol has now been shown to be incorrect and the experimental results of Irvine and Patterson to have been wrongly interpreted.

That monoacetone mannitol could not be written as (II) was first pointed out by Müller (*Ber.*, 1932, **65**,

1055) who showed that this monoacetone mannitol could be obtained by debenzoylation of 1 : 6-dibenzoyl monoacetone mannitol and that it gave a ditrityl derivative. Therefore, the acetone residue in this monoacetone mannitol could not possibly engage a primary hydroxyl group, and it was suggested that the acetone group was attached to C_3 and C_4. This was proved correct by Brigl and Grüner (*Ber.*, **1933**, **66**, 931) who oxidised the tetrabenzoyl mannitol, which Fischer (*Ber.*, **1915**, **48**, 266) had prepared from the monoacetone mannitol of Irvine and Patterson, with lead tetra-acetate and obtained dibenzoyl *d*-glyceraldehyde. Further confirmation came from the work of H. O. L. Fischer and Appel (*Helv. Chim. Acta*, 1934, **17**, 1574) who oxidised monoacetone mannitol to acetone dihydroxysuccinic dialdehyde which they subsequently converted into *l*-tartaric acid. From all this evidence there can be no doubt that the monoacetone derivative of mannitol obtained by Irvine and Patterson has the acetone group attached to the hydroxyl groups of C_3 and C_4, (III).

α-Diacetone mannitol has not been studied as extensively and its structure, as 1 : 2-3 : 4-diacetone mannitol, suggested by Irvine and Patterson, rests on no very firm basis. Experiments have now been carried out which prove its constitution more rigidly. The α-diacetone mannitol has been prepared in a yield of 34%, and has been oxidised to diacetone aldehydo-*d*-arabinose. Gatzi and Reichstein (*Helv. Chim. Acta*, 1938, **21**, 914) obtained a similar compound from diacetone arabinose diethyl mercaptal and recorded its having $[\alpha]_D$ −34° whereas the compound now described had $[\alpha]_D$ −14·4°.

Hydrolysis of the diacetone aldehydo arabinose from diacetone mannitol proceeded smoothly, and *d*-arabinose, identical with an authentic specimen, was obtained. These experiments prove beyond doubt that in α-diacetone mannitol the acetone residues are attached to C_1, C_2, C_3, and C_4, but since, in monoacetone mannitol, the acetone residue is certainly attached to C_3 and C_4 and since the monoacetone compound can be obtained by the further hydrolysis of the diacetone mannitol, it follows that in the latter substance the precise attachment of the acetone residues is to $C_1 : C_2$ and $C_3 : C_4$. (Obviously, owing to the symmetrical nature of the mannitol molecule, the acetone residues could equally well be said to be attached to $C_3 : C_4$ and to $C_5 : C_6$.) Also, since 1 : 2-3 : 4-diacetone mannitol is produced by partial hydrolysis of triacetone mannitol, the latter compound must be 1 : 2-3 : 4-5 : 6-triacetone mannitol (IV). It follows also that the precise structure of diacetone aldehydo-*d*-arabinose is 2 : 3-4 : 5-diacetone aldehydo-*d*-arabinose (V).

To conform to the normal mode of writing the mannitol molecule, the formulations given in this discussion involve what may seem to be *trans* ketal linkage. Rotation can occur about any of the bonds in the mannitol chain so that *cis* ketal formation is always possible, a fact not realised apparently by Irvine and Patterson (*loc. cit.*) at the time their work was published.

The degradative experiments on diacetone mannitol here described constitute a synthesis of *d*-arabinose from mannitol. An improved method of obtaining 3 : 4-monoacetone mannitol is also described.

Experimental.

1 : 2-3 : 4-*Diacetone Mannitol.*—Triacetone mannitol (60 g.) (m. p. 69—70°) [prepared in 75% yield by shaking mannitol (80 g.) in acetone (1 l.) with concentrated sulphuric acid (8 c.c.) overnight followed by the usual method of isolation] was dissolved in 70% alcohol (1200 c.c.) containing concentrated hydrochloric acid (4 c.c.) and the solution warmed at 40—45° for 60 minutes. The acid was neutralised with barium carbonate, the filtered solution evaporated to dryness, and the residue extracted with acetone. The acetone extract, on evaporation, gave a residue which was dissolved in a little alcohol and poured into water, when unchanged triacetone mannitol (26·3 g.) was precipitated. Evaporation of the filtrate and extraction of the residue with benzene gave, after cooling the solution, crystals of 3 : 4-monoacetone mannitol (4·5 g.) (m. p. 86—87°). The mother liquors were evaporated and the resulting syrup, after distillation at 135—145° (bath temp.)/0·03 mm., had $n_D^{15°}$ 1·4630. It was 1 : 2-3 : 4-diacetone mannitol (10·1 g., 34·5% of the theoretical based on the weight of triacetone mannitol hydrolysed). The distillate crystallised on cooling and was recrystallised from ether–ligroin. It had m. p. 37° (yield 8·9 g.); Irvine and Patterson (*loc. cit.*) give the same m. p.

3 : 4-*Monoacetone Mannitol.*—Triacetone mannitol (10 g.) was dissolved in 70% acetic acid (200 c.c.) and the solution heated at 40° for 1½ hours. During this period the rotation of the solution changed as follows : $[\alpha]_D$ +13·6° (initial value); +17·2° (½ hour); +18·4° (1 hr.); +18·4° (1½ hrs.). The solution was evaporated as rapidly as possible at 40—50° under diminished pressure. The residue was extracted with acetone, leaving mannitol (0·7 g.) undissolved. Evaporation of the acetone solution gave a syrup which completely crystallised and which, on being recrystallised from benzene, gave 3 : 4-monoacetone mannitol (6 g.), m. p. 86—87° (80%). Irvine and Patterson (*loc. cit.*) record m. p. 85° for monoacetone mannitol but do not record a yield. Fischer and Appel (*loc. cit.*) record a yield of 45% of the theoretical by hydrolysis with ethanolic hydrogen chloride.

Oxidation of 1 : 2-3 : 4-*Diacetone Mannitol with Lead Tetra-acetate.*—Diacetone mannitol (3 g.) was dissolved in benzene (40 c.c.) and lead tetra-acetate (6·5 g.), suspended in glacial acetic acid (20 c.c.), added and the mixture allowed to stand at 0° for 24 hours. The mixture was poured into water and extracted with more benzene; the benzene extract was washed with sodium bicarbonate and with water, dried over anhydrous magnesium sulphate and evaporated to a syrup (1·1 g.) which was distilled at 80° (bath temp.)/0·03 mm. The product (0·8 g.) had $[\alpha]_D^{19°}$ −13·5° (*c*, 1·187), $[\alpha]_D^{17°}$ −14·4° (*c*, 7·2) in chloroform, $n_D^{23°}$ 1·4421. The liquid restored the colour to Schiff's reagent and was diacetone aldehydo arabinose (Found : C, 57·3; H, 7·5. Calc. for $C_{11}H_{18}O_5$: C, 57·2; H, 7·8%). Gatzi and Reichstein describe diacetone aldehydo-*d*-arabinose as boiling at 84°/0·03 mm. and having $[\alpha]_D$ −34° in chloroform.

*Hydrolysis of Diacetone Aldehydo-*d*-arabinose.*—Diacetone aldehydo arabinose (0·54 g.) was heated at 100° for 2 hours with N-sulphuric acid (10 c.c.). After neutralisation with barium carbonate, filtration and evaporation, a solid was obtained which on recrystallisation from absolute methanol gave crystals of *d*-arabinose (0·28 g.), m. p. 159°, not depressed by admixture with an authentic specimen. It had $[\alpha]_D^{17°}$ −140·6° (initially) changing to −102° (after 24 hours) in water (*c*, 1·338). *d*-Arabinose is described as having m. p. 159—160° and $[\alpha]_D$ −105° (equilibrium value).

The A. E. Hills Laboratories,
The University, Edgbaston, Birmingham.

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5. *Rare-earth Metal Oxides. Part I. The Direct Oxidation of Praseodymium and Terbium Sesquioxides.*

By Joseph K. Marsh.

Repetition of work by Prandtl and Rieder gave no evidence for the existence of quinquevalent praseodymium. Sesquioxides and dioxides form solid solutions, and dioxide formation by praseodymium and terbium is promoted by admixture with sesquioxides of metals with larger apparent ionic radii, provided *C*-type sesquioxide structure be maintained. Otherwise the shrinkage in lattice size on dioxide formation, by causing stronger mutual oxygen repulsion, inhibits quantitative dioxide formation. *A*-Type sesquioxides, being unable to form solid solutions with praseodymium dioxide, inhibit its formation. Praseodymium monoxide mixed with thoria may be prepared by high-temperature reduction.

Although several of the rare-earth metals have been reported to form oxides in which they show a valency higher than three, the evidence except in the cases of cerium, praseodymium and terbium is very unsatisfactory. These three have been commonly supposed to yield quadrivalent oxides, but even this has been called in question by Prandtl and his co-workers, in the case of praseodymium, and a valency of five postulated; the author cannot, however, confirm their experimental findings.

The dioxides of the rare earths where formed belong to the face-centred cubic (fluorite) type of crystal structure. Only cerium, however, has a definite ionic quadrivalency, and cerium dioxide is an almost colourless material. On the other hand, praseodymium and terbium, which form no quadrivalent ions in solution, give dark-coloured higher oxides. This may be attributed to a valency equilibrium or a partial ionic bonding. The rare-earth sesquioxides show only colours arising from the incomplete *N*-shell level characteristic of each of the elements. They mostly have a cubic crystal lattice of 32 metal atoms per unit cell built up on the pattern of the calcium atoms in 8 fluorite cells, each metal atom being surrounded by 6 oxygen atoms occupying approximately 6 of the 8 cube corner positions of the fluorine atoms in the fluorite cell. Highly distorted octahedra of oxygen are thus formed, which are of two types according to whether the vacant cube positions are on face or solid diagonals (Pauling and Schappell, *Z. Kryst.*, 1930, **75**, 128). This close resemblance in structure between dioxide and sesquioxide permits of solid solution between the two. The *C*-type sesquioxide lattice is in fact a subtraction lattice of fluorite type with slight modification. It is stable over an ionic radius ratio range $R_M/R_O = 0{\cdot}53$—$0{\cdot}86$. The upper limit is reached about Sm_2O_3 in the rare-earth series, and for larger ratios (0·86—0·92) found in La_2O_3 and other early members of the series a hexagonal layer *A*-type of lattice is formed. However, Lohberg (*Z. physikal. Chem.*, 1935, *B*, **28**, 402) finds that even La_2O_3 can give indications of *C*-type; and Nd_2O_3 and Pr_2O_3 (Bommer, *Z. anorg. Chem.*, 1939, **241**, 272) can give definite *C*-type oxides. Equilibria rather than sharp transitions between the forms appear to be general. Only oxides capable of forming *A*-type lattice appear to slake and give true hydroxides.

The oxygenation of terbium and praseodymium in presence of other rare-earth metal oxides, and with thorium dioxide, has now been investigated. Work on similar lines has been done by Prandtl and Rieder (*Z. anorg. Chem.*, 1938, **238**, 225). Their results, however, are at some variance with those now reported, the most serious discrepancy being their recording of experiments which they took to be evidence of quinquevalence for praseodymium. Repetition of part of the work which led to this conclusion failed to afford any evidence for a valency greater than four, although rather higher oxygenation had been found than they record when conditions give a value under four. The results for yttrium–praseodymium oxides heated at 350° under different pressures are compared in Table I.

Table I.

Ratios of O : Pr_2O_3 *taken up by* Pr_2O_3 *in admixture with* Y_2O_3.

Ratio	Gas and pressure (atm.). Air, 1.		Oxygen, 1.		Oxygen, 3.	Oxygen, 15.
Y_2O_3/Pr_2O_3.	M.*	P. and R.	M.	P. and R.	M.	P. and R.
2	0·92	0·86	0·96	1·09	—	1·14
5	—	1·00	—	1·24	1·00	1·57
7	—	1·11	—	1·61	1·00	1·71
9 or 10	—	1·03	—	1·41	1·00	1·80

(A value 1·00 represents quantitative production of PrO_2.)

* Present author.

Yttrium oxide after heating in hydrogen, for some reason not accounted for, was found by the author to be quite abnormally hygroscopic, and Prandtl and Rieder mention no adequate precautions against absorption of atmospheric moisture. They used the same sample of oxide repeatedly. Any exposure to air would result in an accumulation of water, for, from the work of Weiser and Milligan (*J. Physical Chem.*, 1938, **42**, 673), it is evident that a temperature of 550° is necessary to desiccate Y_2O_3. It will be seen that in dilute solution in yttrium oxide PrO_2 is formed quantitatively, but there is no evidence for a higher oxide.

All Prandtl and Rieder's results, except the above, can be interpreted with the aid of our knowledge of crystal structures. Praseodymium oxide obtained by ignition in air under a wide range of conditions is Pr_6O_{11}. In the presence of lanthanum oxide, Prandtl and Rieder found that with small amounts of lanthanum (up to

$3Pr_2O_3 + 2La_2O_3$) there is an increase in the degree of oxygenation of the praseodymium, but larger amounts of lanthanum cause a rapid fall. With neodymium the results were similar, but the fall was less. With samarium and gadolinium, the initial rise was again encountered but there was no subsequent fall, perhaps indeed a further small rise. These results may be interpreted as follows. The oxygenation of the praseodymium–lanthanum oxide mixture depended upon the maintenance of the *C*-type fluorite-type oxide. At first, on admixture of lanthanum, formation of $4PrO_2,Pr_2O_3$ (*i.e.*, Pr_6O_{11}) gave way to $4PrO_2,La_2O_3$, with consequent rise in total oxygenation and maintenance of a cubic lattice, but with larger quantities of lanthanum the hexagonal *A*-type lattice appeared which could only take up praseodymium in a tervalent state. Finally, with $9La_2O_3 + Pr_2O_3$ the *A*-type lattice predominated and dioxide formation practically ceased. Owing to the greater stability of *C*-Nd_2O_3 the effect was less marked in this case. With Sm_2O_3 and Gd_2O_3, there being no tendency to form *A*-oxide, no fall occurred. Results recorded later show that these oxides readily allow of quantitative PrO_2 formation.

The influence of cerium on the formation of PrO_2 has occasioned diverse observations. Cerium compounds decompose at temperatures so much below those of other rare-earth salts that cerium dioxide probably forms comparatively large aggregates in oxide mixtures and complete solid solution is not brought about except with intense and prolonged ignition. For example, in Debray's nitrate fusion process for separating cerium, cerium dioxide can be precipitated with very little other rare earth in solid solution, because cerium dioxide will form at 250° by oxidation and decomposition of cerous nitrate, whereas other tervalent nitrates will not decompose much below 400° (see Part II, following paper).

A series of measurements of the gain in weight of mixtures of praseodymium and of terbium oxides with twice their equivalent quantities of other earths has been made, and is shown in Table II. This ratio was selected as being likely best to demonstrate the influence of the diluent earth on the quadrivalent earth, and to give close to maximum oxygenation in all cases.

TABLE II.

Degree of oxidation to dioxide of praseodymium and terbium in admixture with 2 atomic proportions of other elements, in air and in oxygen at 350° or 330°.

		Wt. of mixed reduced oxides.	Increase for $Pr_2O_3 \longrightarrow PrO_2$.					Wt. of mixed reduced oxides.	Increase for $Tb_2O_3 \longrightarrow TbO_4$.				
				Found in 1 atm. of						Found in 1 atm. of			
				air,		oxygen,				air,		oxygen,	
Metal, M.	Ionic radius, A.	$Pr_2O_3 + 4ThO_2$, g.	Calc., mg.	mg.	%.	mg.	%.	$Tb_2O_3 + 4ThO_2$, g.	Calc., mg.	mg.	%.	mg.	%.
Th	1·10	1·3435	15·5	—	—	15·4	100	1·0866	12·2	—	—	8·7	71
		$Pr_2O_3 + 2M_2O_3$.						$Tb_2O_3 + 2M_2O_3$.					
La	1·22	0·9286	15·2	9·2	60	9·9	65	—	—	—	—	—	—
Pr^{IV}	1·00	—	—	—	—	—	—	—	—	—	—	—	—
Pr^{III}	1·16	—	—	—	67 *	—	78 †	—	—	—	—	—	—
Nd	1·15	0·9441	15·4	14·3	93	15·2	99	0·8295	12·8	11·4 *	89	12·0	94
Sm	1·13	1·0020	15·2	15·3	100	15·3	100	—	—	—	—	—	—
Gd	1·11	0·9443	14·4	14·2	99	14·4	100	0·8625	12·8	11·1	87	11·2	88
Tb^{IV}	0·89	—	—	—	—	—	—	—	—	—	—	—	—
Tb^{III}	1·09	—	—	—	—	—	—	—	—	—	50 *	—	67 †
Y	1·06	0·8009	15·6	14·3	92	14·9	96	0·6475	12·7	9·6	73	10·6	84
											23 †		77 †
Yb	1·00	1·0813	15·5	11·9	77	13·3	86	0·8411	12·0	6·7	56	8·0	67

* Established products. † Prandtl and Rieder's findings.

It is found in both instances that with increase in apparent ionic radius of the admixed element there is an increase in dioxide formation provided *C*-type structure be maintained. The influence of *A*-oxide gives poor oxygenation of praseodymium admixed with lanthanum. Some *A*-influence is also found with neodymium. Samarium, gadolinium and thorium allow full oxygenation of praseodymium. In the case of terbium the quadrivalent tendency is less strong than with praseodymium. The slight tendency of neodymium to form *A*-oxide will be lessened in presence of terbium, but increased in that of praseodymium as the latter is itself *A*-forming. Thus neodymium oxide is the most favourable medium for the peroxidation of terbium, but not for praseodymium. Thorium and gadolinium have very similar ionic radii but thorium is a less favourable peroxidising medium than the latter. This is attributable to the lower resistance offered to the introduction of further oxygen by the less oxygen-saturated lattice of the gadolinium oxide. The lattice size is normally the resultant of the electrostatic attraction of opposite charges and the repulsions of like charges. In non-stoicheiometric oxides these forces must be in unstable equilibrium. This arises through a valency equilibrium readily displaceable towards ionic or co-ordinate. In general, positive ions decrease in size on passing to higher valency states. This is seen in the case of the terbium oxides. The sesquioxide unit cube has $a = 10{\cdot}70$, but Tb_4O_7 has $a = 5{\cdot}20$ or $10{\cdot}40$ A. Thus, exercise of a higher ionic valency by terbium is countered by repulsive forces between oxygen atoms, and in air, oxidation above Tb_4O_7 does not occur, and oxygen gas pressure has a large effect on the state of equilibrium. It follows also that if the lattice size can be prevented from contracting on peroxidation, oxygenation will become greater. This is what has in fact been found experimentally. The promotion of higher oxide formation is facilitated in lattices of large size and not, as might at first sight appear probable, by lattices of dimensions to fit most correctly the quadrivalent ion. The

electron field of the metal holds 8 oxygen atoms better at a distance than close to. The bonds have become more covalent in character.

An interesting observation was made when heating thorium and praseodymium oxides. On reduction in hydrogen the black oxide formed a yellow-green powder, which on reoxidation gave the theoretical increase in weight for the change $Pr_2O_3 \longrightarrow 2PrO_2$. Strong ignition in hydrogen, however, caused the green powder to lose further weight and again become black. The increase in weight on reoxidation was then found to be double the previous, and it appears that PrO was formed at the high temperature. Similar experiments with thorium–terbium and thorium–neodymium oxides failed to give evidence of TbO or NdO. The author has shown (*J.*, 1942, 398) that praseodymium possesses an appreciable degree of bivalency. It appears probable that the cubic form of PrO_2 was retained on reduction in solid solution with ThO_2, and was thus capable of undergoing further reduction not possible with pure hexagonal Pr_2O_3. The oxides PrO_2, ThO_2, and BaO all have cubic oxides of similar lattice size.

Experimental.

Rare-earth mixtures were prepared by precipitating oxalates from the requisite quantities of mixed nitrate solutions and igniting them. This did not prove satisfactory with thorium mixtures, however, and for these, hydroxide precipitation was used. Each oxide mixture was then ignited at a bright red heat in a porcelain boat in a silica tube for ½—1 hour, then transferred to a Pyrex tube and heated in a stream of dry hydrogen at 600—700° behind another boat filled with cerium dioxide. The cerium dioxide was partly reduced in the back half of the boat, but traces of oxygen kept the front half from reducing. The traces of water vapour resulting, however, did not appear to cause weighable errors in the oxides. The praseodymium or terbium dioxides in the mixtures underwent reduction. The boat when cool was placed in a small weighing tube with minimum exposure to air. Subsequently it was heated in another tube in air or oxygen for 1½—2 hours at 350° for praseodymium mixtures, and 330—340° for terbium mixtures. The air was passed over soda–lime, sulphuric acid, and phosphoric oxide before use. The increase in weight was then determined.

Yttrium oxide was found to be very hygroscopic, and a blank experiment at 3 atm. pressure of oxygen gave an increase of 0·4 mg. on 1·4 g. of oxide. The rate of increase of the same sample in its boat on exposure to air in the balance case was 6 mg. in the first 5 minutes. In the five experiments with Pr–Y mixtures conducted at 3 atm. of oxygen pressure, 6·83 g. of oxides, calculated to gain 52·3 mg. by the transformation $Pr_2O_3 \longrightarrow 2PrO_2$, gave an increase of 53·8 mg., or after application of the blank correction 51·8 mg., showing as close a correspondence to theory as could be expected. The pressure was obtained by blowing off cylinder oxygen under a head of mercury. Other oxides except that of neodymium are less hygroscopic than yttrium, and blank corrections were not necessary. All the results obtained, once the technique had been proved satisfactory, are recorded in Table II, with the exception of one giving a value of 105% for praseodymium dioxide in neodymium oxide in oxygen. The high value was undoubtedly due to the hygroscopic nature of the neodymium oxide and insufficiently short atmospheric exposure during transfers. A third experiment exactly confirmed the recorded result.

Inorganic Chemistry Laboratory, University Museum, Oxford. [*Received, September 5th*, 1945.]

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6. *Rare-earth Metal Oxides. Part II. A New Study of Oxide Precipitation by Nitrate Fusion.*

By Joseph K. Marsh.

At 450—500° praseodymium oxide forms solid solutions either with hexagonal lanthanum oxide or with cubic ceric and neodymium oxides. In nitrate fusions as previously conducted cerium dioxide was precipitated at low temperatures and was thus rendered unavailable to partner praseodymium dioxide in the latter's precipitation at higher temperatures. More effective separation of lanthanum and praseodymium by nitrate fusion is brought about by putting the mixed earth nitrates into an already fused alkali nitrate mixture. The resulting nascent cerium dioxide then carries down a large proportion of praseodymium dioxide. Still better results are obtained if anhydrous cerous nitrate is added to a cerium-free melt of earth and alkali nitrates. Methods of estimating neodymium and praseodymium by means of the Hilger "Spekker" absorptiometer are described.

When a mixture of cerium-group nitrates is fused with sodium and potassium nitrates at 300—350° cerium dioxide is precipitated almost pure, though not quite quantitatively. When the temperature is raised to 360—400° the rest of the cerium is precipitated accompanied by small amounts of neodymium and praseodymium, but practically without lanthanum. At 410—460° didymium oxide is precipitated, and several days' fusion at 460° will precipitate nearly all the didymium and much of the lanthanum (Debray, *Compt. rend.*, 1883, **96**, 823; Dennis and Magee, *J. Amer. Chem. Soc.*, 1894, **16**, 649; Esposito, *Proc.*, 1906, **22**, 20; Schutzenberger, *Compt. rend.*, 1895, **120**, 663, 1143). The earths are thus precipitated in the order of their basicity, and previous work has demonstrated the possibility of (1) separating cerium from the other earths, (2) separating lanthanum from praseodymium rapidly, provided initially the lanthanum does not constitute more than 33% of the mixture (Brauner, *Proc.*, 1898, **14**, 71; 1901, **17**, 66; *Coll. Czech. Chem. Trav.*, 1933, **5**, 279); (3) rapidly obtaining lanthanum almost pure but only in small yield (Urbain, *Ann. Chim. Phys.*, 1900, **19**, 225).

The present study is undertaken with a knowledge of the crystal structure of the various oxides not possessed by previous investigators, and already referred to in Part I (preceding paper). Cerium and didymium oxides, despite the ease with which they are separable by nitrate fusion, form solid solutions with a cubic structure, whereas lanthanum oxide has a hexagonal structure. The low temperature at which cerous nitrate decomposes to ceric oxide points to the probability of a basic ceric nitrate being formed as an intermediate. If no ceric salt was formed the stability of cerous nitrate would be comparable with other cerium-group nitrates. Cerium oxide,

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however, is formed from nitrate at a temperature so low that the other nitrates are quite stable, and so it separates pure, and its influence on the subsequent nitrate–oxide system is largely eliminated. Now praseodymium, and to a lesser extent, neodymium oxide in the presence of lanthanum may take the lanthanum oxide hexagonal structure. This was discussed in Part I. Lanthanum oxide, on the other hand, does not appear to have much capacity for assuming the cubic structure of CeO_2 or Sm_2O_3, etc. The removal of cerium at the first stage of the nitrate fusion is therefore disadvantageous to the separation of lanthanum and praseodymium as it removes a cubic crystal-forming influence which can be used to promote formation of praseodymium oxide in its cubic form, and so assist its separation from hexagonal lanthanum oxide.

Two new methods of carrying out the nitrate fusion have therefore been investigated. (1) The rare-earth nitrates, mixed with alkali nitrates, are added to already fused alkali nitrates a little at a time so that a nearly constant temperature is maintained; finally pure cerous–alkali nitrate may also be added. (2) Cerium is completely eliminated from the other nitrates, which are then fused with alkali nitrates. In this condition a basic nitrate of the rare earths is formed, and the melt becomes very thick and pearly in appearance. Oxide is formed only at a high temperature (500°), but when cerous and alkali nitrates are added to the thick paste there is immediate reaction and fluidity is restored: basic nitrate → normal lanthanum nitrate + Nd_2O_3 + PrO_2 + CeO_2. The quantity of cerium required to effect the separation of didymium and lanthanum is moderate, and the separation achieved is most satisfactory. Initially, the cerium reacts with the full concentration of other earths in place of a low concentration by the first method. By either of these methods cerium and didymium oxides are co-precipitated and a better extraction of didymium from lanthanum is achieved than by Debray's original method in which cerium oxide is removed from the system early in the fusion. In suspension it can still influence the system, however, as seen by its effect in preventing the formation and separation of the basic nitrate formed in its absence, but it cannot readily enter into solid solution and thus influence the type of oxide formed at high temperatures. No attempt is here made to achieve the most economic conditions of working (*e.g.*, time of heating, temperature at various stages, or proportions of sodium and potassium nitrates), but it is demonstrated that the basicities of neodymium, and even more of praseodymium oxides may vary according to the oxides with which each is associated, *i.e.*, with the crystal structure which they assume. The fusion of nitrates will consequently rapidly separate the rare earths into cubic and hexagonal oxide forms, but solid solution effects and labile states prevent a sharp separation of the elements being thereby achieved.

In carrying out nitrate fusions on mixed cerium earths it has been found that praseodymium behaves as an intermediate between neodymium and lanthanum. This indicates that there is no appreciable ionic quadrivalency of praseodymium called into play. If there was, praseodymium would behave more like cerium and act as a weaker base than neodymium. It must therefore be supposed that the reactions respectively take the courses $Ce^{\cdots} \longrightarrow Ce^{\cdots\cdot} \longrightarrow CeO_2$ and $Pr^{\cdots} \longrightarrow Pr_2O_3 \longrightarrow PrO_2$. The presence of CeO_2, however, has been shown to produce a marked influence on the balance $Pr_2O_3 + O \rightleftharpoons PrO_2$, stabilising PrO_2 formation and thus enabling a separation of praseodymium from lanthanum to be effected.

$$Ce(NO_3)_3 \begin{cases} \nearrow CeO_2 + Pr_2O_3\ (\text{cubic}) + O \longrightarrow PrO_2 \\ \searrow NO_3' + Pr_2O_3\ (\text{hexagonal}) + La(NO_3)_3 \longrightarrow Pr(NO_3)_3 \end{cases}$$

Pr_2O_3 appears to be very labile between cubic and hexagonal forms at 450—500°. If in a lanthanum–praseodymium nitrate mixture there is a good preponderance of praseodymium, on fusion with alkali nitrates nearly pure PrO_2 will precipitate, but if lanthanum exceeds about 33% no separation has heretofore been brought about (Brauner, *loc. cit.*). The lanthanum content in a praseodymium preparation has now been found to be reduced from 12% to about 2% in one fusion; also by throwing cerous nitrate into a lanthanum-rich (87%) mixture, it is now possible without using an undue amount of cerium to obtain 96% lanthanum from the melt, and a high concentration of praseodymium in the CeO_2 residue obtained on lixiviation. A good proportion of PrO_2, but little lanthanum, was coprecipitated with the CeO_2, and the praseodymium could of course be separated subsequently from the cerium by any of the well-known methods. Pure praseodymium nitrate yields on fusion PrO_2, and the cubic form results whenever dioxide formation is possible, but in the absence of cerium only a little lanthanum is required to hold praseodymium oxide in the hexagonal form at the temperatures of nitrate fusions.

Experimental.

Nitrate fusions were conducted in a 300-watt electric furnace built to fit a 100-ml. beaker. Temperatures recorded are uncorrected readings of a glass thermometer (a reading 17° low was found at 420°, the m. p. of zinc).

Estimation of Neodymium and Praseodymium with the Hilger "Spekker" Absorptiometer.—Nitrate solutions and 1-cm. cells were used, and for neodymium the Ilford green light filter 604. No interference by other cerium earths was encountered, and estimations between 0 and 100 g./l. were possible with an accuracy of 1 g./l. Praseodymium was estimated with both Ilford yellow and orange filters 606 and 607 used together, and a water setting of 0·50. Light transmission was rather low, but estimates between 0 and 100 g./l. with an accuracy of 2 g./l. were possible. Some slight overestimate of praseodymium seemed likely when neodymium was also present, and the following method was later adopted. Filters of neodymium nitrate solution (400 g./l. of Nd_2O_3) free from all praseodymium were used. On the left side of the instrument it was found possible to accommodate two cells 0·9 and 1·1 cm. thick, and on the right one cell 3·3 cm. thick. The Ilford violet filter 601 was also used. Only a sharply cut band of light λλ 4540—4340 was transmitted, the intensity being fair. In the middle of this spectral region falls the broadest and strongest of the visible praseodymium absorption bands, having its head at λ 4440. A correction for the amount of neodymium present was required, the effect of neodymium being about 3% of that of praseodymium. The calibration curve for praseodymium was far from a straight line. Sensitivity fell off rapidly above 30 g./l. of Pr_2O_3, but from 0 to 30 g./l. Pr_2O_3 could be

estimated to ±1 g./l., the optimum concentration being about 20 g./l., giving an accuracy of ±5% on the praseodymium estimate. In order to ensure that no ceric cerium was present, solutions were treated with one drop of saturated oxalic acid solution before use. The absorptiometer affords a quick and easy means of estimating neodymium and praseodymium in admixture with a degree of accuracy and delicacy suitable for most purposes.

Purification of Praseodymium.—The starting material was a praseodymium oxide containing Nd_2O_3, 0·5; CeO_2, 1·5; La_2O_3, 11%. Praseodymium oxide (1 part) was converted into nitrate, and potassium and sodium nitrates (5 parts each) were added and fused at 300—350°. Ceric oxide was removed after lixiviation of the cooled melt. Re-fusion at 440° caused production of pearly green scales, presumably of a basic nitrate, and brown fumes and much thickening. After 80 mins. the temperature was raised to 460°, and darkening started after thickening had reached a maximum. After 2·5 hours and heating to 480°, a clear green melt could be decanted fairly well from the black precipitate. A further 45 mins. heating at 500° gave better decantation and a nearly colourless melt. The whole was treated on cooling with water and filtered. The filtrate was precipitated with alkali and yielded 1·45 g. of La_2O_3 (pale brown). The precipitate was well stirred with dilute acetic acid. From the resulting acetate solution 1·6 g. of oxide were recovered. This was pale brown and contained about 16% of La_2O_3 (by arc spectrum). The residue (6·1 g.) contained 1—2% of La_2O_3 (arc estimation). It was very dense and black.

Other mixtures of lanthanum and praseodymium were also separated. One containing about 70% of praseodymium gave three fractions: 2·9 g. of 97·5%, 1·1 g. of 72%, and 2·1 g. of 27·5% Pr_2O_3 (absorptiometer estimates). A sample of nearly pure praseodymium oxide gave 7·5 g. of Pr_6O_{11} with feeble lanthanum arc lines, 1·6 g. of acetic acid extract with less than 1% of lanthanum, and 1·4 g. of oxide not precipitated from the melt with a lanthanum content of 1%. A second treatment of the main precipitate, however, still gave a product in which lanthanum arc lines were detected.

Attempted Separation of Praseodymium from Lanthanum by Simple Nitrate Fusion.—Lanthanum oxide (80%) with praseodymium oxide (14%) and ceria (6%) was converted into nitrate and fused with mixed nitrates as before. The ceria precipitate was removed by lixiviation and filtration after fusion at 350°; a second fusion was given in which a final temperature of 580° was reached. There was darkening to a chocolate-brown towards the end, and the pasty melt regained fluidity. On lixiviation, a brown scaly precipitate was separated (6·8 g.) which dissolved in acetic acid leaving a small brown residue (0·4 g.). This mostly dissolved in concentrated nitric acid, leaving 75 mg. of cerium oxide. The whole of the rare earth was found to have been precipitated from the melt. Nearly all the precipitate being soluble in acetic acid, no separation of lanthanum and praseodymium was here effected. The small fraction insoluble in acetic acid but soluble in nitric acid was found to contain 34·5% of Pr_2O_3, but the experiment confirms previous observers' reports of the impossibility of separating praseodymium from lanthanum when it is a minor constituent by this form of nitrate fusion proceedure.

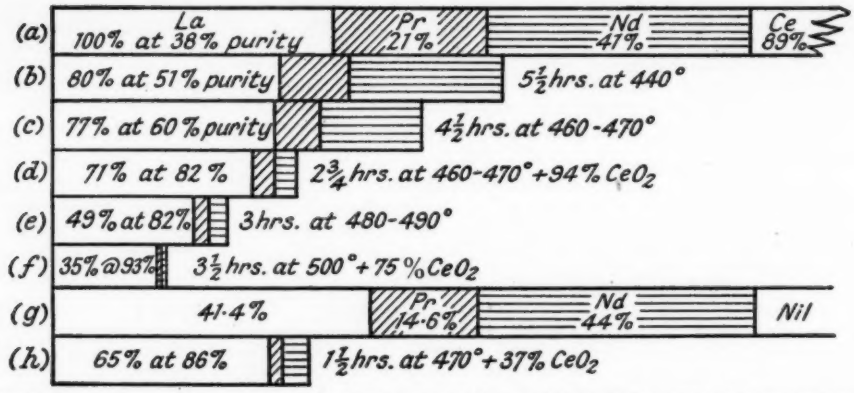
Separation of Praseodymium from Lanthanum with the Aid of Cerium.—17 G. of oxide (Pr_2O_3, 18; La_2O_3, 82%) were made into nitrate, potassium and sodium nitrates (50 g. of each) added, and the whole fused at 440—450° for 3 hours during which a cold powdered cake, containing the equivalent of 7 g. of CeO_2, of fused cerous, potassium and sodium nitrates was added, causing a precipitate in the melt. On lixiviation this was separated. The solution was evaporated, and the fusion, with the addition of cerous and alkali nitrates, twice repeated, the final heating being at 470°. The precipitate obtained by the first lixiviation was partly dissolved in dilute acetic acid. The remainder was brought into solution with nitric acid and hydrogen peroxide, and the cerium removed from the neutral solution by means of potassium permanganate and sodium carbonate ($KMnO_4 + 4Na_2CO_3$). The rare earth, mainly praseodymium, was recovered. The precipitates from the second and the third fusion were not extracted with acetic acid, but were at once treated to remove cerium. There were thus obtained the following products which were examined and estimated by the "Spekker" absorptiometer:

	Oxide, g.	Pr_2O_3, %.	Pr_2O_3, g.
First fusion precipitate: Soluble in HOAc	0·44	65	0·29
Insoluble in HOAc	1·50	70	1·05
Second fusion precipitate	1·20	55	0·66
Third fusion precipitate	1·80	29	0·52
Remainder held in melt	11·4	4	0·45
Total	16·34	—	2·97
Input	17·0	—	3·0

Hence, addition of cerous nitrate equivalent to 21 g. of CeO_2 to 14 g. of lanthanum oxide mixed with 3 g. of praseodymium oxide yielded 11 g. of lanthanum oxide mixed with 0·45 g. of praseodymium oxide; or with the addition of 14 g. of CeO_2 and two fusions only, the recovery of praseodymium was 66% at a concentration raised from 18% to 64%.

Separation of Lanthanum and Didymium in Crude Cerium Earths.—Some crude earths from cerite (approx. La_2O_3, 20; Pr_2O_3, 11; Nd_2O_3, 22; CeO_2, 47%, or reckoned as cerium-free oxides, La_2O_3, 38; Pr_2O_3, 21; Nd_2O_3, 41%) were converted into nitrates and fused with mixed nitrates (2 parts each). Portions of the resulting melt were added portion-wise to a melt of $KNO_3 + NaNO_3$, the temperature being held steady. A series of trials were made, the same crude nitrate but different fusion temperatures being used. On each addition to the melt there was a rapid decomposition with liberation of brown fumes, and a fine precipitate was formed. Each cooled melt was finally lixiviated with a minimum of water, for otherwise the precipitate tended to become colloidal. The crude lanthanum remaining in solution was collected as double potassium sulphate, converted into nitrate, and estimated absorptiometrically. In this series of experiments praseodymium was estimated by means of its absorption in the orange-yellow region, and results may be slightly high. They are shown graphically: (*a*) represents the composition and quantity of the starting material, and (*b*)—(*f*) that of the unprecipitated earth recovered as double sulphate in the series of experiments at the temperatures indicated; (*g*) represents the starting material for the experiment (*h*) when no cerium was originally present in the rare earth. As experimental temperatures were raised, fuller precipitation occurred and purer lanthanum was left, but at 480—490° the yield of lanthanum was down to 50% of input at a purity a little over 80%. Best results were obtained at a temperature of 460—470° with addition of some pure cerous nitrate at the end. The yield of lanthanum was thus raised to 70% at a purity of over 80% starting from 38%. In experiment (*h*) the equivalent of 10·7 g. of oxide was fused with 70 g. of alkali nitrates. Decomposition occurred rapidly above 420° and the melt thickened. It was heated to 500° but remained pasty and darkened only slightly. 16 G. of mixed cerous and alkali nitrates were added (=4 g. of CeO_2), and finally the temperature was held at 470° for 15 mins. The whole reaction occupied 90 mins. A detailed analysis is given below:

		Nd_2O_3,		Pr_2O_3,		La_2O_3 (by diff.),	
	Total, g.	g.	%.	g.	%.	g.	%.
Input	10·7	4·72	44 ± 1	1·56	14·6 ± 1	4·42	41·4
Output, precipitate	6·9	4·00	58 ± 1	1·38	20·1 ± 1	1·52	22
„ retained in melt	3·44	0·30	9 ± 0·25	0·16	4·75 ± 0·25	2·88	86·25



Hence, 65% of the lanthanum was recovered with a purity raised from 41% to 86%. This is a rather better separation than was obtained in experiment (*d*) despite the fact that the cerium used represents only 0·37 part of the cerium-free weight of earths in place of 1·83 parts in (*d*), where much of the cerium was originally in admixture with the other earths.

INORGANIC CHEMISTRY LABORATORY, UNIVERSITY MUSEUM, OXFORD. [*Received, September 5th*, 1945.]

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7. *Rare-earth Metal Oxides. Part III. Their Precipitation from Potassium Hydroxide Melts.*

By JOSEPH K. MARSH.

Rare-earth hydroxides are peptised in KOH,H_2O, and on desiccation at high temperatures and with oxidising conditions PrO_2 and TbO_2 are the first oxides to be precipitated. The cerium earths may be precipitated crystalline, but not always anhydrous. Thus the good separation obtainable of praseodymium from neodymium is attributed in part to isomorphism of PrO_2 and NdO(OH) and solid solution with *C*-form Nd_2O_3. These three are precipitated before *A*-Nd_2O_3. TbO_2 forms solid solutions with Gd_2O_3 or Dy_2O_3, and the Tb^{IV} ion, being small and highly charged, is concentrated in early precipitates, and the elimination of terbium from dysprosium is efficient.

BECK (*Angew. Chem.*, **1939**, **52**, 536) has found that the rare-earth oxides are soluble in fused potassium hydroxide and that in oxidising conditions the higher oxides of praseodymium and terbium may be precipitated from the melts, and a concentration of the two elements thus brought about. PrO_2 collected at the anode on electrolysis of a melt containing a commercial didymium preparation with a 10% praseodymium content. The higher oxide of terbium was precipitated from a melt to which potassium chlorate was added. Praseodymium could also be concentrated by this method. He claims that one fusion raised the terbium content from an initial 1% to 35%, but this conclusion will be criticised later. Complete purification of neodymium he claimed to be possible, but elimination of all neodymium from praseodymium was not accomplished because, he supposed, both praseodymates $Pr(PrO_4)$ and $Nd(PrO_4)$ were formed. Formations of potassium praseodymate and potassium neodymite were also postulated, but no evidence for any of these compounds was advanced.

The author has found that the rare-earth oxides are insoluble in fused anhydrous potassium hydroxide, but the hydroxides possess a solubility of the order found by Beck in fused potassium hydroxide stick of ordinary laboratory type which contains 15—17% of water, and melts about 140° instead of 360° for the anhydrous material. It now appears that when fractionation of mixed earths occurs it is due to their different affinities for water. Weiser and Milligan (*J. Physical Chem.*, **1938**, **42**, 669, 673) have studied the dehydration of hydrous neodymium and praseodymium oxides. They find inflexions in the isobars of each, indicating definite $Nd_2O_3,3H_2O$ or $Nd(OH)_3$ and $Pr(OH)_3$ formation at temperatures of 150—200°, but thereafter praseodymium oxide loses water much more readily than neodymium oxide, so that dehydration of the former at 400° is equal to that of the latter at 600°. Since the dehydrations were done in air, the possibility arises in the case of praseodymium that oxidation took place and PrO_2 was removed from the system, and that the difference between the two isobars is in part due to this side reaction. If this is so under strong oxidising conditions due to potassium chlorate or anodic oxygen in a melt, the differentiation between neodymium and praseodymium behaviour is likely to be still more marked.

The author has studied the precipitation of lanthanum, praseodymium and neodymium oxides from potassium–sodium hydroxide melts and obtained a number of crystalline precipitates. In the case of lanthanum at 290° the precipitate consisted of microcrystalline octahedra with two well-developed square faces. These crystals are clear and colourless. From an impure lanthanum melt they separated side by side with dark PrO_2 octahedra. They lost weight on ignition corresponding to over one molecule of water per La_2O_3, but retained their outward form, and in air they were not carbonated rapidly. At 320—350° the precipitate consisted of prismatic crystals, and at 370—420° of large hexagonal plates easily distinguished with a hand lens. These lost a little weight on ignition but are believed to be *A*-type La_2O_3, which has a hexagonal layer lattice.

Melts of praseodymium at all precipitation temperatures gave only black octahedra of PrO_2. Praseodymium and the other dioxides could not be dissolved in "stick" potassium hydroxide under any conditions. As hydrated praseodymium sesquioxide is dehydrated much more readily than its neodymium analogue and probably also its lanthanum analogue, if dehydrating and oxidising conditions are provided Pr_2O_3 must form first, pass at once into PrO_2 and be precipitated, while the others remain in the melt.

Neodymium melts containing some praseodymium in presence of potassium chlorate gave at low temperatures (320°) large numbers of small brown grains which were only identifiable as octahedra if praseodymium was not too scarce. These are probably solid solutions of PrO_2, NdO(OH) and *C*-Nd_2O_3. The existence of the hydrous oxide NdO(OH) is known (Joye and Garnier, *Compt. rend.*, 1912, **154**, 510; Weiser and Milligan, *loc. cit.*). The latter authors find it to be the only stable hydrous oxide between 300° and 500°. No other rare earth has been reported as giving an analogous compound, and the probability that this oxide hydrate has been mistaken in the past for NdO_2 is referred to later. It is probably isomorphous with PrO_2, and capable of solid solution with *C*-Nd_2O_3. In being precipitated it will thus help to carry down PrO_2. A didymium melt as it loses water appears to precipitate (1) PrO_2, (2) NdO(OH), (3) *C*-Nd_2O_3, (4) one or two forms of *B*-Nd_2O_3, or hydrated forms of *A*-Nd_2O_3, (5) *A*-Nd_2O_3. As (1), (2), and (3) can form solid solutions, the black octahedra of PrO_2 are succeeded by brown amorphous grains, since *C*-oxides are always amorphous; *C*-Nd_2O_3, however, is not the stable oxide form for neodymium at the temperatures of the melts, but requires the stabilisation afforded by solid solution. Thus the brown grains are found mixed with pale blue crystals which obviously contain no PrO_2. These appear to be of two prismatic forms, one having a very limited range of stability and twinning at 90°, the other twinning at 60° often in 6-pointed stars and resembling the 320—350° lanthanum precipitate. Their identity has not been established. Two possibilities seem open: they may be hydrated forms of *A*-Nd_2O_3 or the *B*-forms of Nd_2O_3 of which little is known.

Finally, at high temperatures these forms redissolve and the last fraction of oxide is recovered as large hexagonal plates as in the case also of lanthanum, but here tinted blue. These hexagonal plates have not been observed in the case of elements not known to give *A*-oxides.

In nitrate fusions (Part II, preceding paper) anhydrous melts are encountered and a rapid separation of lanthanum from praseodymium and neodymium takes place on the basis of different oxide crystal forms, but there is little separation of the last two. In potash melts use is made of the differential stability of the oxide hydrates, and the didymium pair separate well. From the work of Weiser and Milligan by analogy with samarium and yttrium oxides it is unlikely that gadolinium and dysprosium oxides form any monohydrate isomorphous with TbO_2 and NdO(OH). All attempts to prepare recognisably crystalline precipitates of these earths from potassium hydroxide melts were failures. The lesser affinity of terbium for a fourth equivalent of oxygen, and the more ready dehydration of gadolinium and dysprosium hydrous oxides, combine to make the separation of terbium less efficient than that of praseodymium. The separation which does occur must take place mainly on account of the insolubility of TbO_2. When through loss of water anhydrous oxide begins to form in the melt, oxidation of Tb_2O_3 takes place and TbO_2 is precipitated. Since with the neighbours of terbium the *C*-oxide is the normal form, and this gives a solid solution with TbO_2, the separation is not sharp, but depends upon the relative solubilities and concentrations of terbium and the other oxides in solution in the melt. It is a case of Goldschmidt's generalisation (J., 1937, 655) that a small highly charged ion separates early in magmatic crystallisations. As a method of separating terbium and gadolinium except on a very small scale, potash fusion compares unfavourably with fractionation of the double magnesium nitrates in presence of bismuth magnesium nitrate; but for the separation of small quantities of terbium which remain obstinately in dysprosium during a dimethyl phosphate fractionation (Marsh, J., 1939, 554) the method proved satisfactory, and it was found possible to prepare a white dysprosium oxide. Four oxide fractions from a melt varied from deep brown to a pale straw colour, showing a remarkable degree of fractionation.

Beck's finding that praseodymium-free neodymium was readily obtained has not been confirmed. One fractionation failed to give any appreciable removal of an initial 8% of praseodymium, and with an initial 15% the purest neodymium retained 5% after one fusion. Whereas, in the case of terbium, fractionation proceeds during the whole course of the operation, since a single solid solution forms the precipitate throughout, yet in the case of didymium as soon as blue hexagonal types of precipitate begin to be formed appreciable further fractionation probably stops. Theoretically it should be possible to help the elimination of praseodymium by adding a naturally *C*-type earth, but the experiment of adding some samaria did not result in any noticeable improvement. Alkali fusion is better adapted to give a very rapid rough separation of praseodymium and neodymium than to prepare the pure products.

The stability of NdO(OH) appears to account for much of the common attribution of a quadrivalency to neodymium, which is often accepted in modern text-books. Brauner (*Coll. Czech. Chem. Comm.*, 1935, **5**, 279), for instance, gently ignited some oxalate and subsequently heated the product in hydrogen and collected $1H_2O$. He therefore claimed that the oxalate yielded Nd_2O_4, whereas it would appear almost certain that it yielded NdO(OH). He admits (Proc., 1901, **17**, 66) that the supposed Nd_2O_4 had no oxidising properties like the other higher oxides in the rare-earth group. Marc (*Ber.*, 1902, **35**, 2370), on the other hand, contended that it had: on addition of CeO_2 to a lanthanum and didymium oxide (15% Pr_2O_3), the available oxygen, measured iodometrically, at first below expectation for quantitative CeO_2 formation, at 2% outstripped theory, and between 5% and 10% outstripped theory for CeO + PrO_2; thus with Ce, 15; Pr, 15%, the dioxide amounted not to

30% but to 45%, and some neodymium dioxide formation was therefore postulated. Marc, however, appears to have used no delicate test for cerium, and there is room for doubt as to whether his didymium mixture was entirely free from cerium. The author made an oxide mixture with neodymium and the above proportions of cerium and praseodymium, all pure oxides, dissolved it in nitric acid, and precipitated it as oxalate; after ignition the oxide contained rather less oxygen than theoretical for full $CeO_2 + PrO_2$ formation. Marc's result was thus not confirmed.

The rare-earth sesquioxides are all soluble in fused "stick" potash, but appear first to become hydrated and less dense. The absorption of water from the potash may even raise the m. p. of the latter so that hard solid lumps of KOH incrusting the rare earth form in a cool melt. For maximum solubility of oxide, water up to a total of about 30% should be present in the alkali, and the oxides are with advantage mixed to a paste with saturated potassium hydroxide before use. If hydroxides are dissolved, additional water is not required. Probably solubilities of oxides increase a little with atomic number. Ytterbium oxide was more soluble than the early members of the series. On lixiviating the cool melt it was obtained in a colloidal state. In general, losses of material were encountered with all the rare earths. These were probably due to non-recovery of unprecipitated hydroxides on lixiviation of melts owing to their passage to a sol condition. These losses at times amounted to 10% and detract from the advantages of the process as applied to valuable materials. Fused sodium hydroxide has little power of dissolving rare earths, probably on account of its weaker affinity for water. Their solubility in potassium hydroxide is low under 250°, but rises rapidly to a maximum roughly at 320°. At this temperature sodium hydroxide is anhydrous, but boiling potassium hydroxide solution contains 16% of water. At slightly higher temperatures, when the KOH,H_2O phase becomes unstable, precipitation of rare earth begins. The m. p. of potassium hydroxide then rises rapidly, but may be kept low conveniently by addition of 10—20% of sodium hydroxide. This assists decantation, and the precipitates are formed at lower temperatures and appear to be more crystalline.

It has been shown in Part I (this vol., p. 16) that terbium in admixture with gadolinium oxide may be oxidised in oxygen to a higher degree than is represented by Tb_4O_7, but not fully to TbO_2. Precipitation of terbium from potash melt is likely to yield an oxide not less oxygenated than by heating in 1 atm. of oxygen. Beck's claim to have produced in one fusion a terbium oxide with 0·25% of active oxygen cannot be said to indicate for certain a terbium content over 6% instead of the 35% suggested (TbO_2 contains 4·2%). Nothing can be assumed as to the state of oxidation which terbium may attain on precipitation from a potash melt. No reliance can be placed upon iodometric estimates of terbium peroxide unless it is known that the terbium is (1) nickel-free, (2) oxidised to a definite state. The first condition is not attained in the original precipitates from potash. For the second condition it is necessary to heat the oxide carefully at 330°, and to know the nature of the diluent earths. Even then there is an ambiguity, for oxygenation probably passes through a maximum value at a particular dilution.

Nickel crucibles become deeply oxidised in contact with moist potash melts, and considerable rare earth is taken up in the oxide coat. This may be dissolved upon the next occasion when the crucible is used, and may cause serious contamination of the new charge. In separating traces of terbium from dysprosium by fractional precipitation, it is therefore essential that a set of crucibles be used in the same sequence: a clean empty crucible from the head must not be used to receive a tail fraction. When ytterbium oxide was dissolved in a potash melt in an oxidised nickel crucible, the nickel oxide was dissolved and the crucible showed bright metal. Iron was rapidly attacked in a potash–ytterbium melt and a green deposit believed to have been $Yb(OH)_2$ was formed. Ytterbium thus appears to be very easily reducible in potash.

The rare-earth hydroxides in moist potassium hydroxide are best regarded as being peptised. Their case is similar to that of the alkaline earths though the solubility is rather less. Salt formation does not appear to play a part. In fact, the quadrivalent oxides which might most conceivably be salt forming are the first to be precipitated from the melts. Further investigation is required to establish firmly all the facts concerning the reactions taking place, and the natures of the interesting products formed in potash melts.

Experimental.

The melts were made in a 300-watt electric furnace built to fit a 100-ml. nickel crucible. Temperatures recorded are readings of a glass thermometer shod with nickel. Electrolysis was carried out with a thick platinum wire cathode dipping slightly into the surface of the melt, the crucible acting as anode, and 4 volts were applied.

Treatment of Crude Dysprosium Material.—The dysprosium gave a dark rust-coloured oxide and contained perhaps 10% of gadolinium in addition to terbium, which, however, by arc spectrum appeared a quite minor constituent. 17·5 G. of dysprosium oxide were dissolved in 75 g. of "stick" potassium hydroxide and 3 g. of potassium chlorate added. Gassing began at 345°, and frothing at 370°. The first precipitate (2·5 g.) was of a deep rust colour, the second (4·5 g.) at temperatures up to 400° was deep red brown, the third (2·9 g.) up to 420° was pale ochre, the fourth (3·0 g.) up to 450° was biscuit-coloured. The final residue amounted to 50% of the alkali and was almost free from rare earth. The oxides as precipitated from alkali were very dense, and darker than after solution and reprecipitation as oxalate. 42 G. of dysprosium oxide were worked up, and the fractions united according to colour. After three fractionations some very dark head fractions were obtained, and small tail fractions of which the last was much paler than Sm_2O_3, indeed practically white. The terbium content could not exceed 0·01%.

Lanthanum.—A clear melt was obtained at 300° by heating a mixture of 50 g. KOH (stick) + 20 g. NaOH + 8 g. H_2O + 10 g. La_2O_3. After 5 mins. and at 310° precipitation started. As it appeared to be exothermic, heating was stopped and the temperature reduced to 290°. After 20 mins. the melt was decanted and a crop of crystals obtained. The melt was reheated at 260—280° for 2½ hours, and good crystals were formed. These were collected and washed with dilute acetic acid. Under magnification they were seen to be octahedral with two strongly-developed square faces.

When less lanthanum was in solution and the temperature of precipitation was higher (310—340°) the crystals were smaller and of indeterminate form. On reheating to 350° acicular crystals showing twinning at an angle of 60° with occasional perfect six-pointed stars were obtained. There were also a few hexagonal plates and roundish specks (dissolving octahedra?). A final heating to 410° gave a crop of good hexagonal plates.

Praseodymium.—The oxide PrO_2 was unattacked by fused "stick" potassium hydroxide but Pr_2O_3 (89%) was dissolved. It gave a colourless melt, which however became greenish on cooling. A mixture of 25 g. KOH + 10 g. NaOH + 2·5 g. H_2O + 4 g. Pr_2O_3 + 2 g. $KClO_3$ at 320—335° gave a clear melt which later formed a skin of shining black crusts, from which it was decanted. Second and third heatings at 350° and 380° gave further crops. There was some frothing at 380°. All the precipitates were seen under magnification to be octahedra. The arc spectra showed a concentration of lanthanum in the later fractions, but it was not striking.

Neodymium.—Oxide containing 8% of praseodymium was dissolved in "stick" potassium hydroxide to give a sky-blue melt. Electrolysis at 340° for ½ hour gave a small dark precipitate. Further electrolysis at 350—380° gave a coarser precipitate, which was collected. Under magnification only brown grains of indefinite form were seen. A third heating without electrolysis gave a crop of good crystals, bluer, and mostly hexagonal plates. The first precipitate lost 1% by weight on ignition, the last only 0·3%. No definite enrichment in praseodymium was found in the first precipitate when examined absorptiometrically.

Didymium.—70 G. of potassium hydroxide ("stick") + 11 g. of earths (Nd_2O_3, 83·5; Pr_2O_3, 15·5; La_2O_3, 1·0%; CeO_2, trace) gave a clear melt at 320°. After 45 mins. of electrolysis, during which the temperature rose to 360°, a brown precipitate appeared suddenly and subsequently darkened to maroon. Electrolysis was stopped after 10 mins. (380°), and after short standing the melt was decanted and the precipitate (1) recovered (1·1 g.). The melt was reheated and 10 g. of sodium hydroxide added. A second crop of precipitate (2) was recovered (3·8 g.). The third heating gave a precipitate (3) brown at first but later blue-grey (1·4 g.). Under magnification crops (1) and (2) were mainly brown grains of indeterminate form, but (2) contained some pale needles. Crop (3) was mainly blue hexagonal plates. After removal of nickel the praseodymium contents were estimated absorptiometrically and were found to be (1) 25, (2) 13, (3) 5%. Only a very little earth remained unprecipitated.

In another similar experiment 1 g. of samarium oxide was added and three precipitates obtained and estimated: (1) 2·7 g., 80% Nd_2O_3, 19% Pr_2O_3; (2) 2·0 g., 79% Nd_2O_3, 19% Pr_2O_3; (3) 1·1 g., 84% Nd_2O_3, 4·5% Pr_2O_3 (11·5% Sm_2O_3 by diff.). The effect of the samarium was to increase the proportion of brown grains, but this was not helpful in concentrating the praseodymium. The recovery of earths is shown much below 100% owing to difficulty in decanting, any hydroxide appearing on lixiviation of residues being lost on washing the precipitate with acetic acid. The effect of a little cerium in the earths is to cause the precipitate to be fine and therefore more easily held in suspension.

Electrolysis of the melts resulted in liberation of hydrogen at the cathode until most of the oxides had been precipitated and the water lost, but finally there was often an indication of metal formation.

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INORGANIC CHEMISTRY LABORATORY, UNIVERSITY MUSEUM, OXFORD. [*Received, September 5th*, 1945.]

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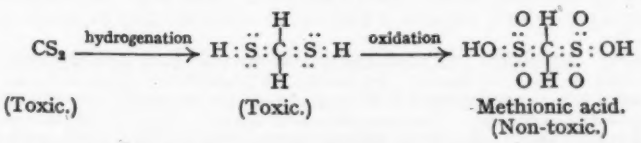
8. *Studies in the Detoxication of Catalyst Poisons. Part IV. Detoxication of Carbon Disulphide.*

By EDWARD B. MAXTED and ARTHUR MARSDEN.

The suppression of the catalytic toxicity of small concentrations of carbon disulphide, contained as a poison in a hydrogenation system catalysed by platinum, has been examined. Complete detoxication of the poison was obtained by the use of reagents containing permolybdic or perphosphoric acid in the presence of an excess of hydrogen peroxide. Hydrogen peroxide alone was less effective. A further study has also been made of the greatly increased detoxication effect obtained by adding the detoxicating reagents in more than one step.

CARBON disulphide is of considerable practical interest as a poison in catalytic hydrogenation, since it accompanies thiophen in technical benzene. Its detoxication has been carried out by the general method used in Parts I, II, and III of this series (*J.*, 1945, 204, 763, 766), namely, by conversion into a "shielded" form in which the normally poisonous sulphur atom loses its toxic character by virtue of the presence of a completely shared electron octet (*J.*, 1940, 252; 1941, 132).

With carbon disulphide, as in earlier work with thiophen, the oxidising reagent was applied after a short period of preliminary hydrogenation, during which the preferentially absorbed poison apparently undergoes preferential hydrogenation to a derivative which, although still toxic and accordingly still obstructively adsorbed by the catalyst, can be more readily oxidised than carbon disulphide itself. Under these conditions, complete detoxication was easily obtained, whereas, if the initial hydrogenation stage is omitted, the detoxication fails. It is probable that the intermediate hydrogenation product formed from carbon disulphide is methylenedithiol, $CH_2(SH)_2$ (Sabatier and Espil, *Bull. Soc. chim.*, 1914, **15**, 228) and that the course of the detoxication is:



In the above scheme the electronic unsaturation and subsequent saturation of the sulphur atoms only are indicated.

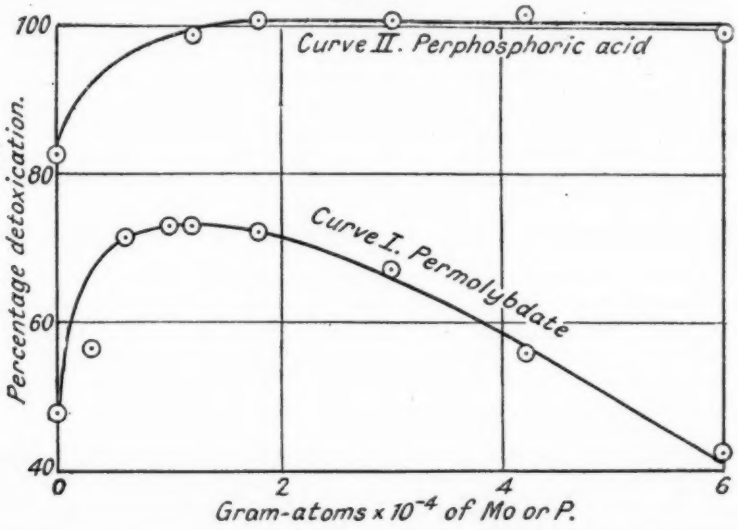
Experimental.

The general technique was similar to that described in earlier papers. The standard hydrogenation charge taken for each run consisted of 0·05 g. of stock platinum-black, suspended in 5 c.c. of a 2N-solution of crotonic acid in acetic acid and poisoned in each case by 10^{-5} g.-mol. of carbon disulphide, the system being made up to a total volume of 10 c.c. by addition of a further 2 c.c. of acetic acid and 3 c.c. of water, including any water or acetic acid added with the poison or with the detoxicant. This amount of carbon disulphide was sufficient, while in its normal toxic state, to poison the catalyst substantially completely.

Before addition of the detoxicants, the system was hydrogenated for 15 minutes, at 27°, for the necessary preliminary reduction of the carbon disulphide. During this initial shaking, a small volume of hydrogen, usually of the order of 2 c.c., was absorbed rapidly in the first minute or so, corresponding not only with the above reduction but also with the clean up of oxygen adsorbed on the platinum catalyst and with solution of hydrogen in the liquid and its adsorption on the catalyst; and the hydrogenation then proceeded at a steady rate of less than 0·1 c.c. per minute, which represents the poisoned rate. The system was then removed from the hydrogenation shaker and detoxicated by addition of a known amount of the detoxicating reagent under the conditions described for each series. After destruction of the excess of detoxicant (per-acid and hydrogen peroxide) by heating, the detoxicated charge was re-connected to the hydrogenation apparatus, and the rate of hydrogenation, at 27°, was measured in order to determine the extent to which the poisoned catalyst had recovered its unpoisoned activity. This original activity, which was determined in blank runs without poison, corresponded with the absorption of hydrogen at the rate of 23·6 c.c. per minute.

Detoxication with Permolybdate.—Detoxication was carried out, as before, by adding dilute aqueous potassium molybdate followed by an excess of hydrogen peroxide to the standard hydrogenation charge containing the poisoned catalyst. Two types of detoxication curve were plotted. In the first, the amount of hydrogen peroxide added was kept constant and the amount of molybdenum salt varied: in the second, the molybdenum content was kept constant and the hydrogen peroxide varied, the detoxication observed being in each case plotted against the variable.

Fig. 1.



Curve I of Fig. 1 gives the result of a series of runs in which the hydrogen peroxide was maintained at 6×10^{-3} g.-mol. (0·2 g.), added in one step, while the molybdate was varied up to a value corresponding with 6×10^{-4} g.-atom of Mo. It will be seen that a maximum detoxication of about 75% was obtained with a little over 1×10^{-4} g.-atom of Mo, and that the detoxication then fell if the molybdenum content was further increased. Since a visible precipitate is formed on adding the larger concentrations of molybdate, this effect (which is similar to that previously observed with peruranates and pertitanates) is probably due to the cloaking of the catalyst by the precipitate. For this reason, the detoxication curves with varying hydrogen peroxide content were determined in the presence of molybdate kept constant at $1{\cdot}2 \times 10^{-4}$ g.-atom of Mo.

Three series of this type are summarised in Fig. 2. In Curve I of this figure, the hydrogen peroxide was added all at once. In Curve II the total amount of peroxide indicated by the abscissæ was added in two, and in Curve III in four, equal increments. The increased detoxicating effect obtained by this stepwise addition, compared with the effect of adding the same total amount all at once, has already been discussed in Part II. It may be noted that, in the runs of Curve II, the system which was being detoxicated was, after each addition of peroxide, heated to 100° and re-cooled to room temperature for the next addition, whereas in Curve III the system was, after the first addition, heated to 80—85° and maintained at this temperature, subsequent additions being made at intervals of about 15 minutes without intermediate cooling. The temperature was, of course, brought down to 27° for the hydrogenation run. It was not practicable, with the small volumes used in the present tests, to add the detoxicant in more than four steps; but the good detoxication obtained under the conditions of Curve III suggests a continuous addition, drop by drop, as an effective detoxication procedure on a larger scale.

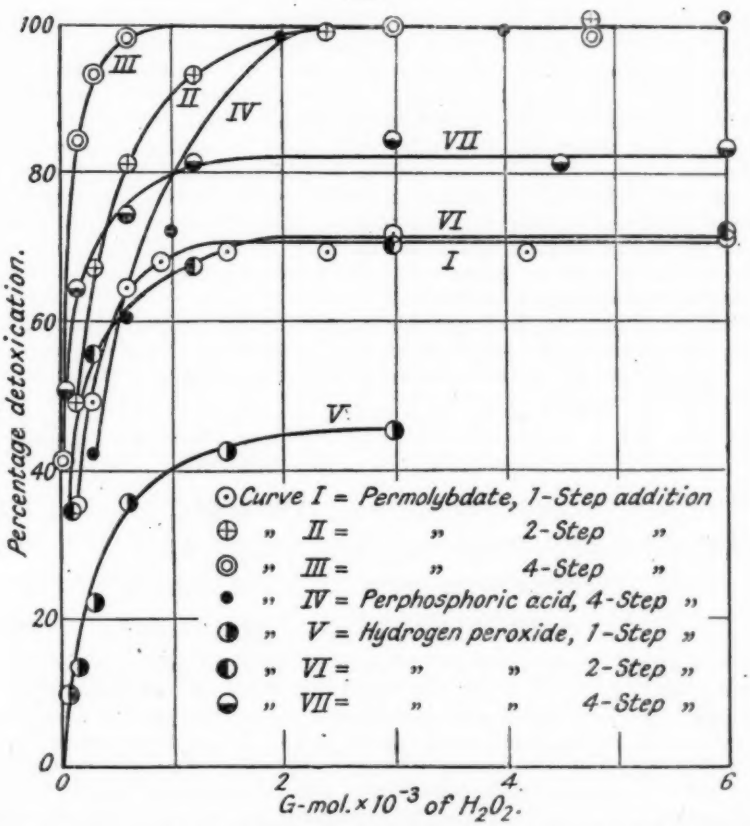
Detoxication by Perphosphoric Acid.—The reagent used (perphosphoric acid in the presence of excess of hydrogen peroxide) was made as described in Part II, namely, by acting on phosphoric oxide with an excess of 30% hydrogen peroxide at 0°, precautions being taken against access of moisture to the pentoxide during the weighing out and at all stages up to its interaction with the peroxide. The reagent could then be diluted with a convenient small quantity of ice-cold water and could be kept for about 2 days at 0° without appreciable loss in its effectiveness as a detoxicant. This allowed sufficient reagent (usually 5 c.c.) for a number of runs to be made up from one weighing of phosphoric oxide.

As before, two types of detoxication curve were plotted. In Curve II of Fig. 1, the amount of the phosphorus component (weighed as P_2O_5) was varied, the total hydrogen peroxide being kept constant at 6×10^{-3} g.-mol., which was

added in four equal increments. It will be seen that complete detoxication was reached with reagent containing about $1{\cdot}8 \times 10^{-4}$ g.-atom of phosphorus (0·013 g. of P_2O_5). Actually, the activity of the detoxicated catalyst was usually slightly above its unpoisoned activity, this being probably due to the cleaning up of small traces of original poison contained in the catalyst itself.

A detoxication series of the second type, in which the phosphorus component was kept constant at 0·01 g. of P_2O_5 ($1{\cdot}4 \times 10^{-4}$ g.-atom P) and the hydrogen peroxide was varied, is summarised by Curve IV of Fig. 2. As in the previous perphosphoric acid series, the peroxide was added in four equal increments, the first addition (as reagent) being made at room temperature and the remaining additions (hydrogen peroxide alone) at 80—85° without intermediate cooling. Complete detoxication was reached at a somewhat higher hydrogen peroxide content than in the corresponding 4-step

FIG. 2.



permolybdate curve (Curve III), namely, at slightly more than 2×10^{-3} g.-mol. of hydrogen peroxide in place of 1×10^{-3} g.-mol.

Detoxication of Carbon Disulphide by Hydrogen Peroxide Alone.—It has been shown in previous papers that hydrogen peroxide, even in the absence of a per-acid, is capable of bringing about some detoxication of cystein and that the effect, although less than that induced by using a suitable per-acid, can be increased by addition in more than one step. Similar results have been observed for the detoxication of carbon disulphide. This is shown in Curves V, VI, and VII of Fig. 2, which relate to this use of hydrogen peroxide by itself and summarise the effect of adding the total amount of peroxide indicated by the abscissæ respectively in 1, 2, and 4 equal steps. In Curve VI (2-step addition), hydrogenation at 27° under standard conditions was carried out between the addition of the two increments in order to allow a point on Curve V (1-step addition) to be determined in the same run. In Curve VII (4-step addition) the first increment was added at room temperature, and the remaining increments at 80—85° without intermediate cooling. The reaching of a maximum detoxication value—in each case well below 100%—which is not increased by a further increase in the total hydrogen peroxide used for the detoxication should be noted, this effect being similar to that previously observed for cystein.

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UNIVERSITY OF BRISTOL. [*Received, October 16th*, 1945.]

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9. *Retention of Asymmetry During the Beckmann, Lossen, and Curtius Changes.*

By A. CAMPBELL and J. KENYON.

(i) The oxime of (+)-α-phenylethyl methyl ketone undergoes the Beckmann transformation into (−)aceto-α-phenylethylamide with almost complete retention of asymmetry.

(ii) (+)Phenylmethylacethydroxamic acid is converted by the Lossen change into (−)-α-phenylethylamine of 99·2% optical purity.

(iii) By Schmidt's modification of the Curtius reaction (+)hydratropic acid is converted into (−)-α-phenylethylamine of 99·6% optical purity.

It is suggested that molecular configuration and asymmetry are retained during these reactions.

It was shown recently that the oxime of (−)methyl γ-heptyl ketone is converted by the Beckmann transformation into (−)acetoheptylamide in what was considered to be an almost optically pure condition (Kenyon and Young, *J.*, 1941, 263). Unfortunately, the optical rotatory powers of these compounds are small, a fact to which attention has been directed by Bernstein and Wallis (*J. Org. Chem.*, 1942, **7**, 262), and it seemed desirable to repeat the reaction with compounds possessing higher rotatory powers.

This has been done, and the following conclusions can be drawn from the results of the work. (i) (+)-α-*Phenylethyl methyl ketoxime* having $[\alpha]_D$ +25·4° (alcohol) is converted smoothly into (−)acet-α-phenylethylamide having $[\alpha]_D$ −167·4° (alcohol); this is in close agreement with $[\alpha]_D$ −168·1°, the specific rotatory power of the optically pure compound obtained by acetylation of (−)-α-phenylethylamine prepared by direct resolution of the *dl*-base. (ii) (+)Hydratropic acid is smoothly converted successively into (+)*phenylmethylacethydroxamic acid*, (+)*benzoyl phenylmethylacethydroxamate*, and potassium benzoyl phenylmethylacethydroxamate. The last compound suspended in boiling benzene decomposes readily to give (+)-α-phenylethyl *iso*cyanate, which, on hydrolysis, yields (−)-α-phenylethylamine having an optical purity of 99·2%. (iii) The azide of (+)hydratropic acid is converted by the Curtius rearrangement into (−)-α-phenylethylamine of 99·3% optical purity (Kenyon and Young, *loc. cit.*). This reaction has been repeated by the more convenient procedure devised by Schmidt (*Ber.*, 1922, **55**, 1571), *i.e.* the addition of sodium azide to a solution of (+)hydratropic and sulphuric acids in chloroform, followed by warming. In this case the resultant (−)-α-phenylethylamine had an optical purity of 99·6%.

Since it has been shown that (+)hydratropamide is converted by the Hofmann reaction into (−)-α-phenylethylamine of 95·9% optical purity (Arcus and Kenyon, *J.*, 1939, 916) it follows that (+)hydratropic acid can be converted into (−)-α-phenylethylamine by several well-known types of molecular rearrangements with almost complete retention of asymmetry.

		Retention of optical activity.	Name of reaction.
(+)Ph·CHMe·CO_2H	→ Ph·CHMe·CO·N_3 → (−)-Ph·CHMe·NH_2	99·3%	Curtius
	→ Ph·CHMe·CO·N_3 → (−)-Ph·CHMe·NH_2	99·6	Schmidt
	→ Ph·CHMe·CO·NH_2 → (−)-Ph·CHMe·NH_2	95·8	Hofmann
	→ Ph·CHMe·C(:NOH)OH → (−)-Ph·CHMe·NH_2...	99·2	Lossen
	→ Ph·CHMe·C(:NOH)Me → (−)-Ph·CHMe·NHAc	99·6	Beckmann

It has been shown that the closely related (+)-benzylmethylacetic acid is converted by (*a*) the Hofmann reaction (Wallis and Nagel, *J. Amer. Chem. Soc.*, 1931, **53**, 2787) and (*b*) the Curtius reaction (Jones and Wallis, *ibid.*, 1926, **48**, 169) into (+)-α-benzylethylamine hydrochloride. It has also been shown that (−)-benzylmethylacetic acid has the same configuration as (−)-α-benzylethylamine hydrochloride [from the (+)amine] (Kenyon, Phillips, and Pittman, *J.*, 1935, 1072). Therefore, it appears highly probable that (+)hydratropic acid and (−)-α-phenylethylamine possess similar configurations, and it follows that, during the rearrangements now described, not only is molecular asymmetry retained but molecular configuration as well.*

Experimental.

dl-*Hydratropic acid*. A suspension of sodamide (47 g.) in dry ether was gradually added to a well-stirred solution of redistilled benzyl cyanide (140 g.) in ether (100 c.c.), and the whole heated under reflux for 3 hours. It was then cooled in ice and, during 4 hours, mixed with methyl sulphate (170 g.); after being stirred for 8 hours, at room temperature, water was added and the ethereal layer separated and dried. The α-phenylethyl cyanide thus obtained (115 g.) had b. p. 110—112°/14 mm. This cyanide (100 g.) was added to a mixture of water (88 c.c.), acetic acid (105 c.c.) and conc. sulphuric acid (115 c.c.); refluxing began spontaneously and was maintained by warming for 3—4 hours. The separated upper layer was washed with water, dissolved in 2N NaOH and the alkaline solution extracted with ether and acidified. The resulting hydratropic acid (84 g.) had b. p. 153—155°/20 mm. (+)Hydratropic acid, m. p. 28°, $a_D^{16\cdot5°}$ +51·71° (*l*, 0·5), was obtained as described by Arcus and Kenyon (*loc. cit.*) who give m. p. 29°, $a_D^{16°}$ +51·81° (*l*, 0·5).

* In a recently available publication Brodskii and Mikluklin (*Compt. rend. Acad. Sci. U.R.S.S.*, 1941, **32**, 558) state that when the reaction product of benzophenone oxime hydrochloride and phosphorus pentachloride is decomposed with water enriched with O^{18} the resultant benzanilide contains O^{18}; these authors conclude therefore that the rearrangement is *inter*molecular so far as the migration of oxygen is concerned.

As the Beckmann change involves two migrations of groups (i) a radical from carbon to nitrogen and (ii) –OH (or –OX) from nitrogen to carbon it is perhaps natural to assume that they together constitute a single molecular rearrangement which may be either *intra*- or *inter*-molecular. Consideration of the results of the Russian investigators together with those now described suggests that the migration of R is *intra*molecular whilst that of OX is *inter*molecular, and subsequent to the initial migration.

It is possible, however, to criticise the use of phosphorus pentachloride in this connexion, since the intermediate product must almost certainly be an oxygen-free compound and therefore the resultant benzanilide necessarily contains oxygen derived from the water used in the hydrolysis. The argument would have been more convincing if a reagent had been used capable of esterifying the hydroxyl group instead of displacing it.

It is perhaps relevant to point out that whilst sulphuric acid converted α-phenylethyl methyl ketoxime smoothly into crystalline acet-α-phenylethylamide (as described above), phosphorus pentachloride converted it into a product which on reaction with water yielded no crystalline material.

Conversion of (+)-α-*phenylethyl methyl ketoxime into* (−)*acet-α-phenylethylamide.* (+)-α-*Phenylethyl methyl ketone.* To a cold ethereal solution of methylmagnesium bromide (from Mg, 1·5 g.) powdered anhydrous cadmium chloride (4·5 g.) was slowly added with stirring and the mixture stirred for 2 hours at room temperature. To this solution of dimethylcadmium, cooled to 0°, was added dropwise during 30 minutes, an ethereal solution of (+)-hydratropoyl chloride (from 7·3 g. of acid). The reaction mixture, after being heated under reflux for 3 hours, was decomposed with dilute sulphuric acid and extracted with ether; the ethereal extract was washed with alkali, dried, and distilled yielding (+)-α-*phenylethyl methyl ketone* (5·0 g.), b. p. 116—117°/12 mm., $[\alpha]_D^{13\cdot7°}$ + 58·21°; $[\alpha]_D^{14\cdot9°}$ + 58·18°; $[\alpha]_D^{16\cdot4°}$ + 58·14° (*l*, 0·5) (Found: C, 81·3; H, 8·4. $C_{10}H_{12}O$ requires C, 81·1; H, 8·1%).

(+)-α-*Phenylethyl methyl ketoxime.* The (+)-ketone (5 g.) was added to a solution of hydroxylamine hydrochloride (2·4 g.) and sodium acetate (2·7 g.) in water (15 c.c.) and alcohol (18 c.c.) and the whole heated under reflux for 4 hours. The resulting *oxime* separated from alcohol in needles, m. p. 96°·(3·1 g.), $[\alpha]_D^{14\cdot5°}$ +25·4° (*l*, 1; *c*, 2·437, ethanol), $[\alpha]_D^{14\cdot1°}$ + 17·4° (*l*, 1; *c*, 2·031, benzene) (Found: C, 73·7; H, 7·8; N, 8·6. $C_{10}H_{13}ON$ requires C, 73·6; H, 8·0; N, 8·6%).

(−)*Acet-α-phenylethylamide.* Conc. sulphuric acid (2·5 g.) was added dropwise to a stirred solution of the (+)-oxime (2·5 g.) in dry ether (50 c.c.) and the mixture heated under reflux for 30 minutes; after evaporation of the ether and addition of ice, a crystalline precipitate of (−)-acet-α-phenylethylamide (1·4 g.) was obtained having $[\alpha]_D^{15\cdot7°}$ −167·7° (*l*, 2; *c*, 2·177), $[\alpha]_D^{15\cdot2°}$ −167·1° (*l*, 2; *c*, 2·094) both in ethanol. It separated from aqueous acetic acid in plates, m. p. 103—104°, alone and mixed with an authentic specimen, prepared by the action of acetic anhydride on (−)-α-phenylethylamine, which had m. p. 104°, $[\alpha]_D^{17°}$ −168·1° (*l*, 2; *c*, 2·117, ethanol).

Conversion of (+)*hydratropic acid into* (−)-α-*phenylethylamine* via *the hydroxamic acid.* (+)-*Phenylmethylacethydroxamic acid.* A solution of (+)-hydratropoyl chloride (5 g.) in benzene (18 c.c.) was added dropwise to a stirred solution of hydroxylamine (2 g.) in benzene (15 c.c.) at 0°; the separated white solid was collected after some hours and crystallised from ethyl acetate in needles (3·8 g.), m. p. 126°, $[\alpha]_D^{17°}$ +20·3° (*l*, 1; *c*, 2·133, water), $[\alpha]_D^{17°}$ +51·5° (*l*, 1; *c*, 5·132, ethanol), $[\alpha]_D^{17\cdot5°}$ +36·4° (*l*, 1; *c*, 2·173 acetone) (Found: N, 8·4. $C_9H_{11}O_2N$ requires N, 8·5%). It gave a cherry-red colouration with aqueous ferric chloride.

The corresponding *dl*-hydroxamic acid, prepared by the same method, had m. p. 119—120° (Found: N, 8·7%).

(+)*Benzoyl phenylmethylacethydroxamate.* Benzoyl chloride (3·5 c.c.) was added in several portions with vigorous shaking to a cold solution of the (+)-hydroxamic acid (3·8 g.) in acetic acid (25 c.c.) and a saturated aqueous solution of sodium acetate (25 c.c.). The precipitated solid was separated, washed with water, and dried under reduced pressure. It separated from ethyl acetate–ligroin in plates (3·5 g.), m. p. 153°, $[\alpha]_D^{17°}$ +39·4° (*l*, 1; *c*, 3·279, alcohol), $[\alpha]_D^{15°}$ +22·3° (*l*, 1; *c*, 2·785, chloroform), $[\alpha]_D^{16}$ +28·6° (*l*, 1; *c*, 2·906, benzene) (Found: N, 5·1. $C_{16}H_{15}O_3N$ requires N, 5·2%).

The corresponding *dl*-benzoyl derivative, prepared by the same method, had m. p. 148° (Found: N, 5·2%).

Potassium benzoyl phenylmethylacetylhydroxamate. A solution of potassium (0·83 g.) in anhydrous methanol (8 c.c.) was added to a solution of the (+)-benzoyl derivative (3·5 g.) in warm acetone (50 c.c.) and the potassium derivative separated as a colourless microcrystalline powder. Anhydrous ether (30 c.c.) was added and the solid (3·7 g.) separated by filtration.

(−)-α-*Phenylethylamine.* The potassium salt (3·7 g.) was mixed with dry benzene (25 c.c.) and heated under reflux for an hour; the suspension was then filtered to remove potassium benzoate. The filtrate * was mixed with conc. hydrochloric acid (5 c.c.), warmed to 45°, and stirred for one hour. After some hours, the aqueous acid layer was separated and rendered alkaline. The liberated (−)-α-phenylethylamine (1·8 g.) had b. p. 72°/12 mm., $[\alpha]_D^{15\cdot6°}$ −18·96° (*l*, 0·5). Its acetyl derivative had m. p. 103—104°, alone or mixed with an authentic specimen, and $[\alpha]_D^{18°}$ −166·9° (*l*, 2; *c*, 2·209) in ethanol.

Conversion of (+)-*hydratropic acid into* (−)-α-*phenylethylamine* via *hydratropic azide* (*Schmidt rearrangement*). Sulphuric acid (10 c.c.) was added to a solution of (+)hydratropic acid (5 g.) in chloroform (40 c.c.); sodium azide (4 g., 1·2 mols.) was then added slowly to the vigorously stirred solution maintained at 45°. After 30 mins., the evolution of nitrogen having ceased, the solution was rendered alkaline and extracted with ether. The resulting (−)-α-phenylethylamine (2·9 g.) had $[\alpha]_D^{14\cdot3}$ −19·04° (*l*, 0·5); by the action of acetic anhydride it was converted into (−)acet-α-phenylethylamide, leaflets from aqueous acetic acid, m. p. 103—104°, alone or when mixed with an authentic specimen, $[\alpha]_D^{17°}$ −165·2° (*l* 2; *c*, 2·499, ethanol).

A parallel experiment, using hydratropic acid having $[\alpha]_D^{11\cdot5°}$ +32·47° (*l*, 0·5), yielded α-phenylethylamine having $[\alpha]_D^{14\cdot2°}$ −11·80° (*l*, 0·5). The optical purity of the acid was 62·1% and of the amine 61·7%; thus, the retention of optical activity was 99·4%.

It was shown by Bernstein and Whitmore (*J. Amer. Chem. Soc.*, 1939, **61**, 1324) that the azide of incompletely resolved (+)hydratropic acid, having $[\alpha]_D^{25\cdot5°}$ +86·1°, was converted by the Curtius reaction into α-phenylethylamine, the benzoyl derivative of which had $[\alpha]_D^{27°}$ −39·2° in benzene; reference to this result ought to have been made in the paper by Kenyon and Young (*loc. cit.*), but these authors much regret they were unaware of it at the time.

The benzoyl derivative of the (−)-α-phenylethylamine obtained by the first Schmidt rearrangement described above had $[\alpha]_D^{16°}$ −41·8° (*l*, 2; *c*, 2·634, benzene) and $[\alpha]_D^{16\cdot5°}$ −149° (*l*, 0·5; *c*, 1·167, carbon disulphide).

Our thanks are due to Dr. D. P. Young for assistance in the early part of this work, to Dr. A. K. Mills for details of the preparation of *dl*-hydratropic acid, to Mr. S. Bance for the analytical data, and to the Directors of Messrs. May & Baker, Ltd., who generously placed laboratory facilities at the disposal of one of us (A. C.).

Battersea Polytechnic, London, S.W. 11. [*Received, August* 31*st*, 1945.]

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10. *Studies in the Polyene Series. Part XXII. Condensations between Methyl Propargyl Ether and αβ-Unsaturated Carbonyl Compounds.*

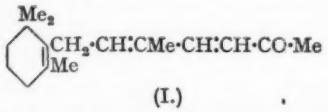
By I. M. Heilbron, E. R. H. Jones, and R. N. Lacey.

Condensations of the Grignard complex from methyl propargyl ether and αβ-unsaturated carbonyl compounds (crotonaldehyde, mesityl oxide, and ethylideneacetone) proceed normally. The methoxy-carbinols (II) thus obtained undergo the expected anionotropic rearrangements in acidic media yielding the isomerides (III), which exhibit light absorption properties corresponding to previous values for conjugated vinylacetylene systems.

* If it be assumed that conversion to α-phenylethyl *iso*cyanate is complete, then this benzene solution contained 1·5 g. in 20 c.c. It had $[\alpha]_D^{15°}$ + 6·19° (*l*, 2; *c*, 7·5); and therefore $[\alpha]_D^{18°}$ + 41·3° is an approximate value of the specific rotatory power of (+)-α-phenylethyl *iso*cyanate.

A similar condensation and isomerisation can be effected by employing the C_{17}-ketone (I), but dehydration of the rearranged product (V) fails to yield materials containing the 5-conjugated system, comparable with that of vitamin A. Migration of the cyclic ethylenic linkage or cyclisation reactions presumably accompany dehydration.

In Part V of this series (Heilbron, Johnson, Jones, and Spinks, *J.*, 1942, 727) the preparation of the C_{17}-ketone (I) was described, and its possible employment for the synthesis of compounds related to vitamin A by condensations with propargyl alcohol or its derivatives was considered. Some preliminary work employing propargyl acetal has already been described (Heilbron, Jones, and Koch, *J.*, 1942, 735), and this paper contains an account of work carried out using methyl propargyl ether. The preparation of the latter from 2 : 3-dibromo-1-methoxypropane has been improved by carrying out the dehydrobromination with potassium hydroxide in glycol solution.

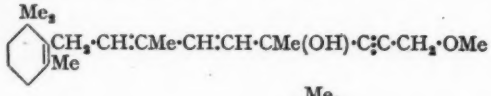


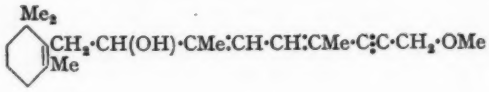
(I.)

$$Me{\cdot}CR_1{:}CH{\cdot}CR(OH){\cdot}C{:}C{\cdot}CH_2{\cdot}OMe \xrightarrow{\text{acids}} Me{\cdot}CR_1(OH){\cdot}CH{:}CR{\cdot}C{:}C{\cdot}CH_2{\cdot}OMe$$

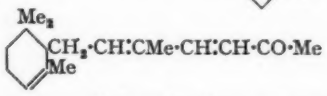
(II.) (III.)

A Grignard condensation between methyl propargyl ether and butaldehyde proceeded satisfactorily (40% yield) and with crotonaldehyde, mesityl oxide, and ethylideneacetone the expected methoxycarbinols (II; R = R_1 = H, R = R_1 = Me, and R_1 = H, R = Me respectively) were obtained in 60, 50, and 25% yields respectively. The last two condensations were effected in cold ethereal solution, a necessary condition in order to prevent undesirable side reactions (Cymerman, Heilbron, and Jones, *J.*, 1944, 145). The various carbinols (II) were all converted into the corresponding rearranged carbinols (III) by keeping them in aqueous acetone containing dilute sulphuric acid, the acid concentration being adjusted in accordance with earlier experience with similar anionotropic rearrangements (Cymerman, Heilbron, and Jones, *loc. cit.*; *J.*, 1945, 90). These carbinols all exhibited light absorption typical of the conjugated vinylacetylene chromophore, described in detail in previous papers in this series.

(IV.) 



(V.)



(VI.)

When the ketone (I), regenerated from its semicarbazone, was treated with an ethereal suspension of the Grignard complex from methyl propargyl ether, a product was obtained which, although too unstable to be purified by high vacuum distillation, must be the expected carbinol (IV). It showed intense light absorption at 2390 A., practically identical with that observed with the ethylcarbinol prepared by condensation of (I) with ethylmagnesium bromide (Part V, *loc. cit.*), and with 0·5% sulphuric acid in an aqueous acetone medium it underwent rearrangement to the more stable *carbinol* (V). Such a 5-carbon anionotropic migration has previously been observed in the case of the ethynylcarbinol from sorbaldehyde (Heilbron, Jones, and McCombie, *J.*, 1944, 134) and the light absorption of (V) ($\lambda_{max.}$ 2810 A.) corresponded with that anticipated for a conjugated dien-yne system. Although the rearranged carbinol (V) can easily be dehydrated, the product, instead of being the desired conjugated tetraen-yne ether contains, according to light absorption indications, at most a trien-yne system. It thus appears that dehydration ensues in such a manner that the double bond in the cyclic system is not brought into conjugation and either rearrangement of this ethylenic linkage into the so-called α-position or cyclisation reactions may be involved. This point will be discussed further in a subsequent communication, where other examples of this behaviour will be described (Part XXIII; in the press).

In the hope of determining the possible fate of the isolated double bond during dehydration reactions the α-C_{17}-*ketone* (VI) has been prepared from the corresponding aldehyde. Its condensation with ethylmagnesium bromide, however, is anomalous and the Zerewitinoff value (0·85 atom of active hydrogen), the light absorption data, and a positive reaction with ketonic reagents indicate that the product is a mixture of carbinols and ketone resulting from 1 : 2-, 1 : 4-, and (possibly) 1 : 6-addition to the conjugated system.

Experimental.

Light absorption data were determined in alcohol.

Methyl Propargyl Ether.—To a solution of sodium (40 g.) in dry methanol (400 c.c.), allyl bromide (200 g.) was added with stirring at such a rate that gentle refluxing occurred, the reaction being completed by heating on the steam-bath. Bromine (270 g.) was then added to the cooled stirred mixture during 2 hours, water was added and on isolation of the product in the usual manner, two fractions were obtained on distillation: (i) b. p. 78—82°/16 mm., $n_D^{20°}$ ranging from 1·49 to 1·51 (120 g.) and (ii) 2 : 3-dibromo-1-methoxypropane (200 g.), b. p. 82—83°/16 mm., $n_D^{20°}$ 1·5123 (Irvine, Macdonald, and Suter, *J.*, 1915, 348, give b. p. 83—84°/17 mm., n_D 1·5143).

The dibromo-ether (200 g.) was slowly added (1·5 hours) to a solution of potassium hydroxide (150 g.) in ethylene glycol (1 litre) contained in a three-necked copper flask, the liquid temperature of the well agitated mixture being kept at 90—100°. After the addition the temperature was raised to 130° and all material with b. p. below 90° was distilled over. The upper layer was separated and dried and, on redistillation through a short column, gave methyl propargyl ether (36 g.), b. p. 63—64°, $n_D^{19°}$ 1·3975 (Bourguel, *Compt. rend.*, 1923, **176**, 752, gives b. p. 63°).

1-*Methoxyhept-2-yn-4-ol*.—To a solution of ethylmagnesium bromide (from 5·15 g. Mg) in ether, dry benzene (200 c.c.) was added and the ether removed by distillation. Methyl propargyl ether (15 g.) in benzene (40 c.c.) was added to the cooled, stirred Grignard reagent during 30 minutes and the mixture gently warmed on the steam-bath for 2 hours by which time the complex had separated as a fine granular white solid. Butaldehyde (16 g.) was added to the cooled, stirred mixture during 20 minutes and the reaction was completed by heating for 2 hours on the steam-bath. The complex was decomposed with saturated ammonium chloride solution and isolation in the usual way gave 1-*methoxyhept-2-yn-4-ol* (11·5 g.), b. p. 76°/4 mm., $n_D^{19°}$ 1·4565 (Found: C, 67·9; H, 9·8. $C_8H_{14}O_2$ requires C, 67·55; H, 9·9%. Active hydrogen (Zerewitinoff): The carbinol (100 mg.) gave 17·6 c.c. of methane at 19°/758 mm., *i.e.*, 1·05 atoms of active hydrogen per mol.). The *α-naphthylurethane* crystallised from ligroin (b. p. 40—60°) in needles, m. p. 66—67° (Found: N, 4·65. $C_{19}H_{21}O_3N$ requires N, 4·5%).

1-*Methoxyhept-5-en-2-yn-4-ol* (II; R = R_1 = H).—Methyl propargyl ether (20 g.) in benzene (40 c.c.) was treated with ethylmagnesium bromide (from 6·8 g. Mg) in benzene (200 c.c.) as above. Crotonaldehyde (20 g.) in benzene (40 c.c.) was added during 15 minutes to the ice-cold stirred reagent and the vigorously stirred mixture was heated to *ca.* 50° for one hour. Isolation in the usual manner gave the *methoxy-carbinol* (23 g.), b. p. 72°/4 mm., $n_D^{20°}$ 1·4795 (Found: C, 68·4; H, 8·5. $C_8H_{12}O_2$ requires C, 68·55; H, 8·65%. Active hydrogen (Zerewitinoff): The carbinol (83 mg.) gave 14·6 c.c. of methane at 27°/765 mm., *i.e.*, 1·0 atom of active hydrogen per mol.). The *α-naphthylurethane* crystallised from ligroin (b. p. 60—80°) in needles, m. p. 75—76° (Found: C, 73·9; H, 6·4. $C_{19}H_{19}O_3N$ requires C, 73·75; H, 6·2%). Light absorption: Maximum, 2230 A.; ε = 66,500.

1-*Methoxyhept-4-en-2-yn-6-ol* (III; R = R_1 = H).—The above methoxy-carbinol (4 g.) was dissolved in the minimum volume of an acetone–dilute sulphuric acid solution (40% acetone, 5% sulphuric acid) and, after the mixture had been kept for 48 hours at 20°, 1-*methoxyhept-4-en-2-yn-6-ol* (3 g.), b. p. 71°/3 mm., $n_D^{19°}$ 1·4976 was obtained (Found: C, 68·8; H, 8·75. $C_8H_{12}O_2$ requires C, 68·55; H, 8·65%. Active hydrogen (Zerewitinoff): The carbinol (95 mg.) gave 14·7 c.c. of methane at 26°/769 mm., *i.e.*, 0·9 atom of active hydrogen per mol.). Light absorption: Maximum, 2280 A.; ε = 13,000. Inflexion, 2340 A.; ε = 10,000. The *α-naphthylurethane* crystallised from ether–ligroin (b. p. 40—60°) in micro-needles, m. p. 65° (Found: N, 4·65. $C_{19}H_{19}O_3N$ requires N, 4·55%). Light absorption: Maximum, 2230 A.; ε = 74,000.

1-*Methoxy*-4 : 6-*dimethylhept-5-en-2-yn-4-ol* (II; R = R_1 = Me).—Methyl propargyl ether (12·5 g.) in ether (100 c.c.) was added to a stirred solution of ethylmagnesium bromide (from 4·2 g. Mg) in ether (200 c.c.) during 20 minutes. After gentle refluxing with vigorous stirring for 2 hours, the mixture was cooled (ice) and treated with mesityl oxide (18 g.) in ether (150 c.c.) and then stirred at 20° for 18 hours. This procedure yielded 1-*methoxy*-4 : 6-*dimethylhept-5-en-2-yn-4-ol* (14 g.), b. p. 76°/3 mm., $n_D^{19°}$ 1·4770 (Found: C, 71·55; H, 9·75. $C_{10}H_{16}O_2$ requires C, 71·4; H, 9·6%. Active hydrogen (Zerewitinoff): The carbinol (102 mg.) gave 15·5 c.c. of methane at 26°/771 mm., *i.e.*, 1·05 atoms of active hydrogen per mol.).

1-*Methoxy*-4 : 6-*dimethylhept-4-en-2-yn-6-ol* (III; R = R_1 = Me).—The above methoxy-carbinol (4·5 g.) was dissolved in the minimum volume of an acetone–dilute sulphuric acid solution (50% acetone, 0·5% sulphuric acid). After 20 hours at 20°, the deep red solution was diluted and extracted with ether from which was obtained 1-*methoxy*-4 : 6-*dimethylhept-4-en-2-yn-6-ol* (4 g.), b. p. 73—74°/3 mm., $n_D^{21°}$ 1·4813 (Found: C, 71·4; H, 9·8. $C_{10}H_{16}O_2$ requires C, 71·4; H, 9·6%. Active hydrogen (Zerewitinoff): The carbinol (97 mg.) gave 14·2 c.c. of methane at 25°/765 mm., *i.e.*, 1·0 atom of active hydrogen per mol.). Light absorption: Maximum, 2280 A.; ε = 13,000.

1-*Methoxy*-4-*methylhept-5-en-2-yn-4-ol* (II; R_1 = H, R = Me).—Methyl propargyl ether (30 g.) in ether (200 c.c.) was added to a stirred solution of ethylmagnesium bromide (from 10·2 g. Mg) in ether (500 c.c.) during 30 minutes, the reaction being completed by gently refluxing for 2 hours. Ethylideneacetone (38 g.) in ether (200 c.c.) was then added to the cooled (ice) stirred mixture (30 minutes) which was then stirred at 20° for 20 hours. This procedure gave the *methoxy-carbinol* (15 g.), b. p. 72°/3 mm., $n_D^{16°}$ 1·4738 (Found: C, 70·2; H, 9·1. $C_9H_{14}O_2$ requires C, 70·1; H, 9·15%. Active hydrogen (Zerewitinoff): The carbinol (162 mg.) gave 27·0 c.c. of methane at 21°/755 mm., *i.e.*, 1·05 atoms of active hydrogen per mol.).

1-*Methoxy*-4-*methylhept*-4-*en*-2-*yn*-6-*ol* (III; R_1 = H, R = Me).—This was prepared by isomerising the preceding carbinol (5·5 g.) in acetone–dilute sulphuric acid (50% acetone, 1% sulphuric acid) at 20° for 48 hours. The rearranged *methoxy-carbinol* (3 g.) had b. p. 73°/4 mm., $n_D^{19°}$ 1·4889 (Found: C, 69·85; H, 9·0. $C_9H_{14}O_2$ requires C, 70·1; H, 9·15%. Active hydrogen (Zerewitinoff): The carbinol (157 mg.) gave 21·6 c.c. of methane at 20°/760 mm., *i.e.*, 0·9 atom of active hydrogen per mol.). Light absorption: Maximum, 2260 A.; ε = 11,500. Inflexion, 2330 A.; ε = 10,500.

7-(2′ : 6′ : 6′-*Trimethyl*cyclo*hexenyl*)-5-*methylhepta*-3 : 5-*dien*-2-*one* (I).—The finely powdered semicarbazone (3 g., Heilbron, Johnson, Jones, and Spinks, *J.*, 1942, 733) was suspended in a mixture of ligroin (250 c.c.; b. p. 60—80°) and 2N-sulphuric acid (70 c.c.) and heated under reflux with stirring for 12 hours. This gave the ketone (2·35 g.), b. p. 75—80°(bath temp.)/10^{-4} mm., $n_D^{18·5°}$ 1·5475. Light absorption: Maximum, 2825 A.; ε = 25,500 (previous values, $n_D^{19°}$ 1·5412 and ε = 22,500).

Condensation of the β-C_{17}-*Ketone* (I) *with Methyl Propargyl Ether*.—Methyl propargyl ether (5 g.) in ether (100 c.c.) was dropped into a cold stirred solution of ethylmagnesium bromide (from 1·35 g. Mg) and the mixture refluxed for 2 hours. The suspension, diluted to about 700 c.c. with ether, was cooled and treated during 20 minutes with a solution of the ketone (2·8 g; constants as above) in ether (50 c.c.), after which the mixture was vigorously stirred and refluxed for 3—4 hours. The product, a viscous orange-coloured oil, had $n_D^{19°}$ 1·5204 (Max. 2380 A.; $E_{1\,cm.}^{1\%}$ 660). The product usually underwent dehydration and/or rearrangement on distillation, but on one occasion it distilled at 85—90° (bath temp.)/10^{-4} mm., as a pale yellow viscous liquid with $n_D^{17°}$ 1·5280 (Max. 2390 A.; $E_{1\,cm.}^{1\%}$ 750, *i.e.*, ε = 24,000 on assumed composition, IV). On other occasions products with much higher *n* values and entirely different light absorption resulted on attempted distillation, *e.g.*, b. p. 90—110° (bath temp.)/10^{-4} mm., $n_D^{14°}$ 1·5570 (Maxima, 2280, 2410, and 3230 A.; $E_{1\,cm.}^{1\%}$ 580, 580, and 480 respectively).

The undistilled condensation product (0·5 g.) was dissolved in acetone–dilute sulphuric acid (200 c.c.; 95% acetone, 0·5% sulphuric acid) and after 20 hours at 19° the product was isolated in the usual way. Distillation gave the rearranged carbinol, 1-*methoxy*-9-(2′ : 6′ : 6′-*trimethyl*cyclo*hexenyl*)-4 : 7-*dimethylnona*-4 : 6-*dien*-2-*yn*-8-*ol* (V) (0·35 g.) as an orange-red viscous oil, b. p. 100—110° (bath temp.)/10^{-4} mm., $n_D^{16°}$ 1·5446 (Found: C, 79·8; H, 10·25. $C_{21}H_{32}O_2$ requires C, 79·7; H, 10·2%). Light absorption: Maximum, 2810 A.; ε = 25,000.

7-(2′ : 6′ : 6′-*Trimethyl*-Δ²′-cyclo*hexenyl*)-5-*methylhepta*-3 : 5-*dien*-2-*one* (VI).—A solution of the crude α-ionone C_{14}-aldehyde (12 g., $n_D^{20°}$ 1·5028; Heilbron, Johnson, Jones, and Spinks, *loc. cit.*) in a mixture of dry pure benzene (600 c.c.) and dry acetone (150 c.c.) together with freshly sublimed aluminium *tert.*-butoxide (18 g.) was refluxed in an atmosphere of nitrogen for 72 hours. The mixture was treated with water (1000 c.c.) and the separated alumina washed with benzene and finally with methanol. The benzene solution was combined with the extracts, washed with water, dried, and evaporated, finally under diminished pressure. Distillation of the residue from an electrically heated retort gave two fractions: (i) bath temp. 40—65°/10^{-4} mm. (2·2 g.), $n_D^{19°}$ 1·5172, chiefly unchanged aldehyde, and (ii) bath temp. 75—80°/10^{-4} mm. (5·2 g.), $n_D^{20°}$ 1·5306. Fraction (ii) was treated with semicarbazide acetate (4 g.) in methanol and the

crude derivative (2·5 g.), m. p. 156—157°, crystallised during some hours. Recrystallisation from aqueous methanol gave the pure *semicarbazone* of (VI) (2·2 g.), as needles, m. p. 162° (Found: N, 14·2. $C_{18}H_{29}ON_3$ requires N, 13·9%). Light absorption: Maximum, 2950 A.; ε = 42,500. Inflexion, 2810 A.; ε = 38,000. The pure semicarbazone (3·3 g.) suspended in ligroin (150 c.c., b. p. 60—80°) was heated on the steam-bath and rapidly stirred in an atmosphere of nitrogen with sulphuric acid (60 c.c., 2N) during 6 hours. The ligroin layer was separated and the aqueous portion extracted three times with ligroin. The combined extracts were washed with sodium bicarbonate solution and water, dried, and evaporated. Distillation of the residue gave the *ketone* (VI) (1·7 g.), b. p. (bath temp.) 75—80°/10^{-4} mm., $n_D^{15°}$ 1·5446 (Found: C, 82·6; H, 10·3. $C_{17}H_{26}O$ requires C, 82·9; H, 10·6%). Light absorption: Maximum, 2825 A.; ε = 24,000. Treatment of the pure ketone with semicarbazide acetate gave the same semicarbazone, m. p. 162°, as that from the crude ketone.

Condensation of the α-C_{17}-Ketone (VI) *with Ethylmagnesium Bromide.*—The ketone (450 mg.) regenerated from its semicarbazone was treated with ethylmagnesium bromide (from 100 mg. Mg) in ether (100 c.c.), the reaction being completed by stirring and refluxing for 2 hours in nitrogen. The product (400 mg.) had b. p. 70—80° (bath temp.)/10^{-4} mm., $n_D^{15°}$ 1·4942 (Found: C, 83·0; H, 11·7. $C_{19}H_{32}O$ requires C, 82·5; H, 11·7%. Active hydrogen (Zerewitinoff): The product (98 mg.) gave 7·2 c.c. of methane at 19°/758 mm., *i.e.*, 0·85 atom of active hydrogen per mol.). Light absorption: Maxima, 2190, 2310, 2380 A.; ε = 5500, 6000 and 6000 respectively.

Since this material gave a positive ketonic reaction with 2 : 4-dinitrophenylhydrazine, a similar undistilled preparation (400 mg.) was treated with Girard's reagent P in the normal manner. The non-ketonic portion, purified by chromatography on alumina, had obviously undergone dehydration since it had $n_D^{16°}$ 1·5230 and a maximum light absorption at 2720 A. (ε = 13,000) and an inflexion at 2820 A. (ε = 12,000).

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IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY, LONDON, S.W. 7. [*Received, September 24th*, 1945.]

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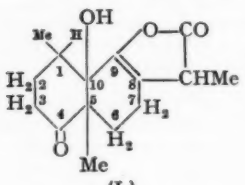
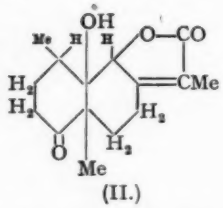
11. *The Constitution of ψ-Santonin. Part I.*

By G. R. CLEMO and WESLEY COCKER.

In addition to *l*-santonin and β-santonin a further compound, $C_{15}H_{20}O_4$, has been isolated from certain species of *Artemesia*. Its chemistry is now discussed, but no final structure can yet be given to the new *compound*, which is named *ψ-santonin*.

IN the course of an examination of a number of species of *Artemesia* collected from the N.W. frontier of India, Messrs. T. and H. Smith, Ltd., of Edinburgh discovered a further crystalline compound in addition to *l*-santonin (III; Clemo, Haworth, and Walton, *J.*, 1929, 2368; 1930, 1110; Clemo and Haworth, *J.*, 1930 2570) and β-santonin (Clemo, *J.*, 1934, 1343).


(I.)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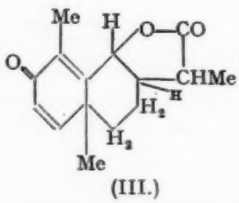
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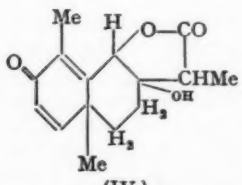

(IV.)

The new compound, $C_{15}H_{20}O_4$, termed *ψ-santonin*, is *lævo*-rotatory. Whilst *l*- and β-santonin impart little colour to concentrated sulphuric acid, ψ-santonin gives an immediate dark brown coloration. Further, *l*- and β-santonin and artemisin (IV; Tettweiler, Engel, and Wedekind, *Annalen*, 1932, **492**, 105) are unaffected by alkaline sodium nitroprusside, but ψ-santonin gives a deep red coloration when the test is performed according to Jacobs and Hoffmann (*J. Biol. Chem.*, 1925, **67**, 333). When, however, the test is modified according to Paist, Blout, Uhle and Elderfield (*J. Org. Chem.*, 1941, **6**, 273) the latter compound gives a pink coloration after the addition of the third drop of sodium hydroxide when the solution is still acid to Congo red, and this colour shows little fading. When the fourth drop of alkali is added and the solution is faintly alkaline to phenolphthalein a deep red coloration is produced which fades after three or four minutes. Addition of further drops of nitroprusside again produce the deep red coloration, which changes to blue-green on acidification. Potassium ferrocyanide has no effect. These results strongly suggest the presence of a β—γ unsaturated lactone.

Tollens' reagent is unaffected by either *l*- or β-santonin, but, like the cardiac aglycones and other α—β unsaturated lactones, a silver mirror is very slowly produced by ψ-santonin. Immediate reduction of the reagent usually takes place with a β—γ lactone (Jacobs, Hoffmann, and Gustus, *J. Biol. Chem.*, 1926, **70**, 1).

ψ-Santonin gives no colour reaction with tetranitromethane, but the absence of ethylenic bonds cannot be concluded from this, since protected or α—β double bonds very often fail to give a reaction with this reagent (Haworth, *Ann. Reports*, 1937, **34**, 328).

Tested side by side, tincture of digitalis and an aqueous-alcoholic solution of ψ-santonin of comparable strength give similar cardiac effects. Depression of conduction and cardiac inhibition take place similarly in each case, but neither *l*- nor β-santonin shows similar reactions. In the latter cases there is slight augmentation of the heart beat, probably due to the alcohol used as solvent. These results point to the existence of an un-

saturated lactone in ψ-santonin (compare Kraft, *Arch. Pharm.*, 1912, **250**, 126; Windhaus, Bohne, and Schwieger, *Ber.*, 1924, **57**, 1388).

ψ-Santonin gives an oxime and a 2 : 4-dinitrophenylhydrazone, but all attempts to prepare a piperonylidene or *p*-nitrobenzylidine derivative have so far failed. Recently, however, it has been possible to obtain a nitrogenous compound, $C_{22}H_{23}O_3N$, presumably a 2 : 3-substituted quinoline by condensation with *o*-aminobenzaldehyde, thereby showing the probable existence of the $-CO-CH_2-$ system. ψ-Santonin has, so far, failed to yield an osazone.

ψ-Santonin is not immediately soluble in sodium hydroxide, but, on shaking, it slowly passes into solution from which it is reprecipitated unchanged even on careful neutralisation with dilute acetic acid. In addition, several attempts to prepare a methyl ester from the sodium salt yielded a substance which gradually lost methyl alcohol and yielded ψ-santonin. The evidence therefore points to the existence of a relatively stable γ-lactone and together with the carbonyl group accounts for three of the four oxygen atoms present in the molecule.

ψ-Santonin yields a monoacetyl derivative with difficulty and in poor yields and this together with Zerewitinoff determinations points to the probable presence of one tertiary hydroxyl group. Incidentally, when the above-mentioned monoacetate is hydrolysed with sodium hydroxide and the solution acidified, a *lactone*, $C_{15}H_{20}O_4$, isomeric but not identical with ψ-santonin is obtained. The structure of this lactone has not been established, but in view of the mobility of tertiary hydroxyl groups it would not be surprising if a molecular rearrangement were to take place during acetylation. No change in structure has yet been encountered when ψ-santonin is treated with potassium hydroxide under a variety of conditions (compare Paist, Blout, Uhle, and Elderfield, *loc. cit.*).

A point of interest is that whilst *l*- and β-santonin are soluble in cold water to the extent of only one part in four hundred and one part in six hundred respectively, ψ-santonin is soluble to the extent of one part in forty, a property which may be due to the hydroxyl group in the last compound.

Catalytic reduction of ψ-santonin by hydrogen in the presence of palladised charcoal and at 1 atm. yields a *dihydro*-compound, $C_{15}H_{22}O_4$, which dissolves readily in sodium bicarbonate with evolution of carbon dioxide and is reprecipitated unchanged even on warming with mineral acid. This dihydro derivative possesses a carbonyl group and it is evident that its preparation involves the hydrogenolysis of the lactone ring. Treatment of the acid with acetic anhydride yields a δ-lactone. Further hydrogenation using Adams' catalyst (PtO_2,H_2O) yields an acid *hexahydro-ψ-santonin*, $C_{15}H_{26}O_4$, which is also produced by reduction of ψ-santonin itself under the same conditions. The latter acid has no carbonyl group and yields a *monoacetyl* compound which is also a δ-lactone. It appears therefore that two of the four additional hydrogen atoms are used in the reduction of the carbonyl group to the corresponding alcohol.

When the reduction of ψ-santonin with Adams' catalyst is carried out quantitatively, it is found that the absorption of the first molecular equivalent of hydrogen is rapid and the second and third equivalents progressively slower.

Dihydro-ψ-santonin is readily reduced with sodium amalgam to an acid *tetrahydro-ψ-santonin*, $C_{15}H_{24}O_4$, which fails to give the reactions of carbonyl compounds but is readily converted to a *monoacetate*, also a δ-lactone. The tetrahydro compound is slowly reduced to the hexahydro compound by Adams' catalyst, and there appears to be no doubt that the reduction of the tetrahydro to the hexahydro compound corresponds to the third (slow) stage in the reduction of ψ-santonin itself. It appears therefore that the first stage in the catalytic reduction is the hydrogenolysis of the lactone ring, the second is the reduction of the carbonyl group, and the third is probably the reduction of the unsaturated lactone.

The hydrogenolysis of unsaturated γ-lactones has been widely investigated by Jacobs and his co-workers and more recently by Elderfield and his co-workers, and it now appears certain that the cardiac aglycones and other β-substituted α—β butenolides undergo hydrogenation by uptake of one molecule of hydrogen to give saturated lactones (Paist, Blout, Uhle, and Elderfield, *loc. cit.*). On the other hand β—γ unsaturated lactones yield varying amounts of deoxy acids on catalytic reduction (Jacobs and Scott, *J. Biol. Chem.*, 1930, **87**, 601) with uptake of two molecules of hydrogen. ψ-Santonin, however, takes up one molecule of hydrogen to yield an unsaturated carboxylic acid, the double bond of which is only hydrogenated with difficulty. This evidence favours the existence of a β—γ double bond, as in structure (I), in which compound there is a " protected " β—γ double bond which might be expected to be resistant to hydrogenation.

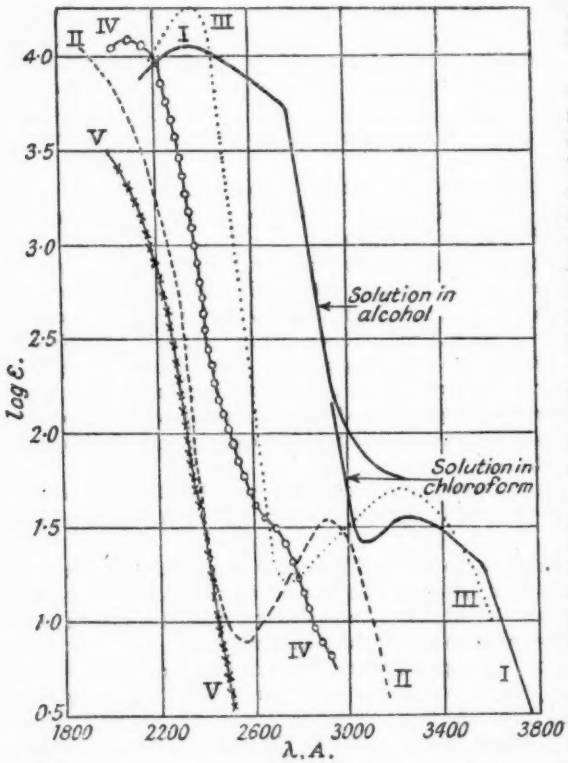
In view of the ready hydrogenation of the double bonds in *l*-santonin using palladised charcoal (Wienhaus and Oettingen, *Annalen*, 1913, **397**, 219; Asahina, *Ber.*, 1913, **46**, 1775), the possibility that the third molecule of hydrogen absorbed in the reduction of ψ-santonin is taken up by a double bond similarly placed to either of those in *l*-santonin is remote, but as α—β double bonds are frequently inert or sluggish towards catalytic reduction (compare Haworth, *loc. cit.*) the evidence cited does not rule out the possibility that this grouping is present in ψ-santonin. Its absence is, however, indicated by spectroscopic studies.

Compounds with such a grouping have an absorption band due to the carbonyl group in the neighbourhood of 3000—3200 A. and a much more intense band (log ε = 3·8 to 4·2) between 2200 and 2500 A. Isolated carbonyl groups absorb near 2800 A. (Gillam and West, *J.*, 1945, 95). *l*-Santonin has absorption bands at 2360 A. (log ε = 4·05) and 3250 A. (log ε = 1·54), corresponding to a carbonyl group conjugated with an α—β double bond (compare Gillam and West, *loc. cit.*, who show that piperitone has bands at 2350 A.; log ε = 4·25, and 3210 A.; log ε = 1·73). On the other hand ψ-santonin shows the band at 2900 A. (log ε = 1·56) charac-

teristic of the isolated carbonyl group, but it has much stronger absorption (no maximum) at 2000—2200 A. (log ε = 2·2—4·0) than would be expected in this case. This spectrum has some similarity to those of β-*cyclo*hexyl-Δ$^{\alpha}$-butenolide and vinyl acetate (see fig.), supporting the conclusion that ψ-santonin possesses an unsaturated lactone ring.

When ψ-santonin is treated with one molecule of bromine it yields a *monobromo* compound, $C_{15}H_{19}O_4Br$, which is readily reduced with zinc and alcohol to ψ-santonin. Three to four molecules of bromine yield a *tribromo* compound, $C_{15}H_{19}O_4Br_3$, which is a lactone and which is reduced in the presence of palladised charcoal to the monobromo compound. Titration by the method of Winkler (*Pharm. Zentr.*, **1924**, **65**, 385) gives a bromine uptake of four atoms which with the above evidence points to the substitution of one bromine atom and the addition of two others to a double bond. Bromination under the conditions of titration points to β—γ rather than α—β unsaturation in the lactone ring.

Dihydro-ψ-santonin on titration by Winkler's method also shows a bromine uptake of four atoms, and it appears that the double bond is preserved during the hydrogenation of ψ-santonin with palladised charcoal, thus supporting the view that only hydrogenolysis of the lactone ring takes place under these conditions of hydrogenation.



I, l-*Santonin*. II, pseudo-*Santonin*. III, *Piperitone*. IV, β-cyclo*Hexyl-Δ$^{\alpha}$-butenolide*. V, *Vinyl acetate*.

When ψ-santonin is treated with 55% sulphuric acid or with anhydrous formic acid at 50°, a dark red solution is quickly produced from which a crystalline compound, $C_{15}H_{18}O_3$, is obtained as the main product. This compound now called *desmotropo-ψ-santonin* is *dextro*-rotatory and like the *dextro*-rotatory derivatives of *l*-santonin is phenolic. It fails to couple with diazotised *p*-nitroaniline and gives only a dull red-brown colour, but it is readily benzoylated and methylated in alkaline solution. It does not give a satisfactory Legal reaction nor is it reduced with palladised charcoal and hydrogen.

Attempts to obtain a fully aromatised compound from desmotropo-ψ-santonin by heating with selenium were unsuccessful; the compound sublimed unchanged. Aromatisation is, however, readily effected by fusion with potassium hydroxide at 320° (cf. Andreocci, *Gazzetta*, **1895**, **25**, 545). The compound obtained has the formula $C_{12}H_{12}O$, corresponding to a dimethylnaphthol, and by analogy with the naphthol obtained from *l*-santonin it was anticipated that it would be a dimethyl-β-naphthol with the methyl groups in the same ring as the phenolic group. It is not identical, however, with 1 : 4-dimethyl-2-naphthol (Cannizzaro and Carnelutti, *Ber.*, 1879, **12**, 1575), which is obtained from *l*-santonin, or with 1 : 3-dimethyl-2-naphthol or with 3 : 4-dimethyl-2-naphthol, both of which have now been synthesised (see Part II, following paper). It was finally shown to be identical with 2 : 4-dimethyl-1-naphthol (Cornforth, Cornforth, and Robinson, *J.*, **1943**, 168), and we are indebted to these workers for a sample of their compound for comparison. It is clear, therefore, that in ψ-santonin there is a carbonyl group at position 4.

When ψ-santonin is treated with cold concentrated hydrochloric acid a *dextro*-rotatory *compound*, $C_{15}H_{22}O_5$, quickly separates. This compound is readily soluble in sodium bicarbonate with evolution of carbon dioxide and is converted into desmotropo-ψ-santonin on treatment with sulphuric acid. Attempts to obtain an oximino derivative gave a high-melting compound which contained nitrogen and apparently also sodium. Further work on the new compound is necessary; the fact that it is *dextro*-rotatory is significant.

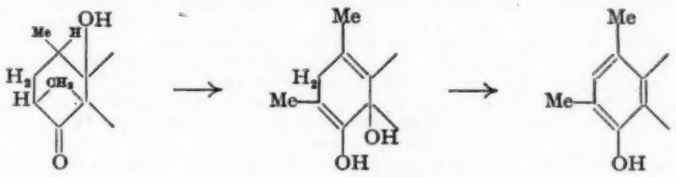
When ψ-santonin, or its dihydro derivative, is distilled with selenium an intractable syrup is produced, but after reduction with amalgamated zinc and hydrochloric acid the dihydro compound yields a gum which, on distillation with selenium, yields an oil whose picrate is identical with that obtained from 1-methyl-7-ethylnaphthalene. This hydrocarbon is also obtained from *l*-santonin (Clemo, Haworth, and Walton, *loc. cit.*) and artemisin (Tettweiler, Engel, and Wedekind, *loc. cit.*). It appears therefore that ψ-santonin possesses a similar carbon skeleton to the compounds named, and that in all three compounds the α-propionyl group is at position 8.

It should be noticed that in the production of 1-methyl-7-ethylnaphthalene a methyl group is lost, which is characteristic of compounds containing angular methyl groups or derivatives of these. This evidence, together with the fact that 2 : 4-dimethyl-1-naphthol may be obtained as indicated above, shows that in ψ-santonin there is a methyl group at position 1 and a methyl group or a derivative of this at either position 5 or 10 and that, during the treatment with acid, the latter methyl group migrates in some way to position 3.

Evidence is presented below to show that the hydroxy group is at position 10 and therefore the angular methyl group is at 5.

The migration of the methyl group from position 5 to position 3 during the treatment of ψ-santonin with sulphuric or formic acids is difficult to explain, as there appears to be no analogy. Migration of methyl groups on treatment of ψ-quinols with mineral acid is well known (cf. Clemo, Haworth, and Walton, *loc. cit.*, who give references to earlier work), but migration takes place to an adjacent position in all the cases mentioned by these workers. In the case of ψ-santonin the methyl group migrates to a position two carbon atoms away.

This difficulty could be overcome by the postulation of a methylene bridge between carbon atoms 3 and 5, in which case simple hydrolysis and dehydration would lead to the required naphthol according to the following scheme.



With such a methylene bridge it would be necessary to postulate a saturated lactone ring, against which there is considerable evidence. The suggested tertiary hydroxyl group may be at positions 1, 5, or 10. It cannot be at 8, as in artemisin, since the lactone is unsaturated, nor can it be at 9 (only possible in the α—β unsaturated lactone structure) because of the ready re-formation of the ψ-santonin after hydrolysis. Furthermore, dihydro-ψ-santonin does not undergo acetylation, but readily gives a theoretical yield of a *lactone*, $C_{15}H_{20}O_3$, on being heated with acetic anhydride, and is regenerated on warming with either dilute sodium hydroxide or dilute hydrochloric acid.

The new lactone is much less stable than ψ-santonin. It gives a *monoxime* on treatment with one equivalent of hydroxylamine, but, with an excess of this reagent, a compound, $C_{15}H_{24}O_4N_2$, is produced which combines the properties of an oxime and a hydroxamic acid. It is also obtained by further treatment of the monoxime with excess of hydroxylamine, and it appears that the lactone ring is opened during this reaction.

Observations on the effect of hydroxylamine on a limited number of γ and δ lactones indicated that the δ-lactones were converted to hydroxamic acids, whilst the γ-lactones were unaffected. Thus, *N*-*p*-toluenesulphonyl-6 : 6-dimethyl-2-morpholone (Cocker, *J.*, 1943, 373) readily gave *N*-*p*-toluenesulphonyl-*N*-β-hydroxy*iso*butylacethydroxamic acid. Coumarin gave β-2-hydroxy-phenylacrylhydroxamic acid, and anhydro-2-hydroxy*cyclo*hexyl-β-propionic acid gave a small yield of a nitrogenous, hygroscopic substance which gave the usual hydroxamic acid reactions. All attempts to obtain a compound containing nitrogen from anhydro-2-hydroxy*cyclo*hexyl-α-propionic acid were unsuccessful and of course ψ-santonin itself gave no hydroxamic acid.

The above evidence supports the view that the lactone, $C_{15}H_{20}O_3$, mentioned above is of the δ-type which could only be the case if the tertiary hydroxy group were at 10. Therefore the angular methyl group is at 5. It should be mentioned that the lactone, $C_{15}H_{20}O_3$, is unaffected by catalytic hydrogenation using palladised charcoal.

The evidence so far presented gives a good picture of the carbon skeleton of ψ-santonin with methyl groups at positions 1 and 5, the keto group at 4, the α-propionyl group at 8 and the hydroxy group at position 10. The position of the double bond in the lactone ring is, however, uncertain, since there is evidence in favour of each possibility, nor is it certain whether fusion of the lactone ring takes place at 9 as in (I) and (II) or in the alternative position 7. On biogenetic grounds and analogy with ψ-santonin, etc., the former is favoured.

Further work in this field is in hand.

Experimental.

ψ-Santonin crystallised from alcohol in colourless rhombic prisms, m. p. 183—184° (Found: C, 68·0; H, 7·7. $C_{15}H_{20}O_4$ requires C, 68·2; H, 7·5%); $[\alpha]_D^{20°}$ — 169° (*c* = 2·49 in chloroform); cell dimensions: *a* = 8·40 A., *b* = 10·1 A., *c* = 15·9 A.; *d* 1·245. The available atomic models did not permit the setting up of accurate scale models of the structures (I) and (II), but measurements made on rough models showed that these structures agreed fairly well with the crystal measurements.

ψ-Santonin dissolved slowly in aqueous sodium hydroxide and was recovered on neutralisation with dilute acetic acid at 0° (Found: equiv. wt. (by titration), 251, 253, 245; *M* (Rast), 275; active hydrogen 1·2—1·3 atoms per molecule. $C_{15}H_{20}O_4$ requires equiv. wt., 264). The *oxime* crystallised from boiling water in long, pointed prisms, m. p. 203—204° (Found: C, 64·8; 64·9; H, 7·5, 7·8; N, 5·0. $C_{15}H_{21}O_4N$ requires C, 64·5; H, 7·5; N, 5·0%). The 2 : 4-*dinitrophenylhydrazone* crystallised from a large volume of alcohol as bright yellow prisms, m. p. 257° (Found: C, 57·3; H, 5·4. $C_{21}H_{24}O_7N_4$ requires C, 56·8; H, 5·4%).

Condensation with o-Aminobenzaldehyde.—ψ-Santonin (0·2 g.), *o*-aminobenzaldehyde (0·1 g.), alcohol (1 c.c.) and sodium hydroxide (0·4 g.; 20%) were shaken together until a clear solution was obtained and then set aside for 48 hours at room temperature. The liquid was diluted with water, extracted thrice with ether and the aqueous portion carefully neutralised with dilute acetic acid. The precipitate was collected, washed with water, dried and recrystallised from dilute alcohol, giving colourless needles, m. p. 210° (Found: C, 75·4; H, 6·4. $C_{22}H_{23}O_3N$ requires C, 75·6; H, 6·6%). This *condensation product* was readily soluble in dilute mineral acid and insoluble in cold dilute sodium hydroxide. It dissolved in the latter on warming and was reprecipitated on neutralisation. The condensation product was undoubtedly a quinoline containing a lactone ring.

Acetyl-ψ-santonin. ψ-Santonin (0·5 g.) was refluxed with acetic anhydride (3 c.c.) and anhydrous sodium acetate

(1·0 g.) for 3 hours. Excess acetic anhydride was removed under reduced pressure and the residue extracted with water and crystallised twice from dilute acetic acid as colourless plates (0·15 g.), m. p. 187°, $[\alpha]_D^{20°}$ − 69·2° (*c*, 2·24 in chloroform) (Found: C, 66·6; H, 7·0. $C_{17}H_{22}O_6$ requires C, 66·7; H, 7·2%). On hydrolysis with dilute sodium hydroxide and crystallisation from dilute alcohol colourless needles were deposited, m. p. 205—207° (Found: C, 67·95; H, 7·59. $C_{15}H_{20}O_4$ requires C, 68·2; H, 7·5%). This new *compound* was not identical with ψ-santonin. *Oxime of acetate*, prepared in alcohol in presence of sodium acetate, crystallised from dilute alcohol as colourless prisms, m. p. 196—197° (Found: C, 63·9; H, 7·1. $C_{17}H_{23}O_4N$ requires C, 63·6; H, 7·1%).

Hydrogenation Experiments.—(a) *Using palladised charcoal.* ψ-Santonin (169·45 mg.) in glacial acetic acid absorbed 17·2 c.c. hydrogen at 16°/755 mm., equivalent to 1·1 mols. hydrogen per mol. In a second experiment, ψ-santonin (4·05 mg.) absorbed 0·50 c.c. hydrogen at 19°/766 mm. equivalent to 1·2 mols. hydrogen per mol. The absorption was complete in 1 hour in each case. (b) *Using Adams' catalyst.* ψ-Santonin (4·56 mg.) absorbed 1·40 c.c. hydrogen at 20°/760 mm. in 1 hour, equivalent to 3·4 mols. hydrogen per mol. In this experiment, a large excess of catalyst was employed. In a second experiment, using a smaller quantity of catalyst, ψ-santonin (327 mg.) absorbed 88·5 c.c. hydrogen at 16°/770 mm. equivalent to 3 mols. hydrogen per mol. of ψ-santonin. The absorption of the first 28·5 c.c. (1 mol.) hydrogen took 15 minutes, the second mol. took 3½ hours and the third mol. took 36 hours.

Dihydro-ψ-santonin. A mixture of ψ-santonin (1 g.), palladised charcoal (0·1 g.) and glacial acetic acid (10 c.c.) was shaken for 20 hours in hydrogen at a pressure slightly greater than one atmosphere. After removal of catalyst and solvent, the residue was crystallised from dilute alcohol as colourless needles (0·9 g.), m. p. 188—189°, $[\alpha]_D^{20°}$ − 239° (*c*, 0·96 in glacial acetic acid), completely soluble with effervescence in dilute sodium carbonate (Found: C, 67·4; 68·1; H, 7·8, 8·0; *M* (Rast) 282. $C_{15}H_{22}O_4$ requires C, 67·7; H, 8·3%; *M*, 266). The same *dihydro* compound was obtained by hydrogenation in alcohol at 100 lbs./sq. in. using palladised charcoal. The quantitative experiments described above using palladised charcoal gave the same compound. The dihydro compound was also obtained by refluxing a mixture of ψ-santonin (0·3 g.), sodium hydroxide (8%, 4 c.c.), ammonia (*d* 0·88, 1 c.c.), water (2 c.c.) and activated copper (2 g.) for 12 hours, cooling and acidifying with dilute acetic acid when, after removal of some brownish flocculent material, the dihydro compound was deposited as well-formed prisms, m. p. 182—184°, raised to 189° by crystallisation from dilute alcohol (Found: C, 67·8; H, 8·8%).

The dry sodium salt of the above acid (2 g.) and methyl iodide (20 c.c.) were refluxed for 24 hours. Excess methyl iodide was removed and the residue extracted with ether and distilled. The fraction b. p. 175—180°/1 mm. was again distilled and collected (1 g.) at 181°/1 mm. On standing, the *methyl ester* solidified and crystallised from ligroin in long, transparent needles, m. p. 77° (Found: 68·6; H, 8·1. $C_{16}H_{24}O_4$ requires C, 68·6; H, 8·6%).

The *oxime of dihydro-ψ-santonin* crystallised from alcohol in short stout prisms, m. p. 229—230° (Found: C, 64·6; H, 7·8; N, 5·0. $C_{15}H_{23}O_4N$ requires C, 64·1; H, 8·2; N, 5·0%). The same compound resulted from the catalytic reduction of ψ-santoninoxime and it reverted to dihydro-ψ-santonin on treatment with hydrochloric acid.

Anhydro-dihydro-ψ-santonin. A mixture of dihydro-ψ-santonin (0·2 g.), acetic anhydride (3 c.c.) and anhydrous sodium acetate (0·5 g.) was heated for 2 hours, excess acetic anhydride removed, the residue extracted with water and crystallised from dilute alcohol, forming colourless needles (0·1 g.), m. p. 158° (Found: C, 72·65; H, 7·8. $C_{15}H_{20}O_3$ requires C, 72·6; H, 8·1%). It was insoluble in sodium carbonate, but slowly dissolved in sodium hydroxide from which dihydro-ψ-santonin was recovered on acidification. The lactone was also obtained by heating dihydro-ψ-santonin for a few minutes at 190—200°.

Oximes of anhydro-dihydro-ψ-santonin. A mixture of the above lactone (0·2 g.), hydroxylamine hydrochloride (0·2 g.; 4 mols.), anhydrous sodium acetate (0·5 g.) and alcohol (3 c.c.) was shaken for 12 hours. The alcohol was removed under reduced pressure and the residue was extracted with water and crystallised from aqueous alcohol as colourless prisms, m. p. 209—210° (decomp.). It gave an insoluble copper salt with ammoniacal copper sulphate, and was insoluble in sodium bicarbonate and, generally, gave reactions of a *hydroxamic acid* (Found: C, 60·7; H, 7·9; N, 9·3. $C_{15}H_{24}O_4N_2$ requires C, 60·8; H, 8·1; N, 9·5%). Using only one molecule of hydroxylamine hydrochloride the true *oxime* was obtained, and this crystallised from benzene–ligroin as colourless needles, m. p. 188° (Found: C, 68·3; H, 7·9. $C_{15}H_{21}O_3N$ requires C, 68·4; H, 8·0%).

Hexahydro-ψ-santonin. A mixture of ψ-santonin (0·5 g.), glacial acetic acid (15 c.c.) and Adams' catalyst (0·1 g.) was shaken in hydrogen at 15 atm. for 24 hours and the product was crystallised from dilute acetic acid as long needles, m. p. 191—192° (Found: C, 66·5; H, 9·8. $C_{15}H_{26}O_4$ requires C, 66·6; H, 9·6%). It readily dissolved in sodium carbonate with effervescence, and was regenerated unchanged on acidification. It did not yield an oxime. *Acetyl-anhydro-hexahydro-ψ-santonin* was obtained by refluxing the hexahydro compound with an excess of acetic anhydride. It crystallised from alcohol as colourless needles, m. p. 125° (Found: C, 69·9; H, 8·75. $C_{17}H_{26}O_4$ requires C, 69·4; H, 8·8%). It was insoluble in sodium hydroxide and was hydrolysed to hexahydro-ψ-santonin with 13% methanolic potash.

Tetrahydro-ψ-santonin. To dihydro-ψ-santonin (0·3 g.) in alcohol (4 c.c.) alcohol-washed 4% sodium amalgam (11 g.) was added in portions. The mixture was refluxed for 5 hours and left overnight. Alcohol was removed and the residue dissolved in water and acidified. The precipitate was crystallised twice from water and obtained as colourless prisms, m. p. 189—190° (Found: C, 67·3; H, 8·8. $C_{15}H_{24}O_4$ requires C, 67·2; H, 9·0%). All attempts to obtain an oximino derivative failed. *Acetyl-anhydro-tetrahydro-ψ-santonin* crystallised from dilute alcohol in colourless prisms, m. p. 104° (Found: C, 70·4; H, 8·3. $C_{17}H_{24}O_4$ requires C, 69·9; H, 8·2%). It yielded the acetyl anhydro-hexahydro compound described above when submitted to hydrogenation in presence of Adams' catalyst.

Tribromo-ψ-santonin. Bromine (1 g., 3 mols.) was added dropwise to a stirred solution of ψ-santonin (0·5 g.) in chloroform (10 c.c.) at room temperature. Stirring was continued for half an hour and the chloroform and excess bromine were removed under reduced pressure. The residue was crystallised from alcohol as long, colourless needles (0·6 g.), m. p. 243° (Found: C, 36·0; H, 3·6; Br, 48·3. $C_{15}H_{19}O_4Br_3$ requires C, 35·8; H, 3·8; Br, 47·7%). *Monobromo-ψ-santonin*, obtained in a similar manner, using 1·2 mols. of bromine, crystallised from ligroin (b. p. 80—100°) as colourless needles or prisms, m. p. 198—199° (Found: C, 52·3; H, 5·5. $C_{15}H_{19}O_4Br$ requires C, 52·4; H, 5·5%). The same monobromo compound was obtained when a solution of the tribromo compound in glacial acetic acid was submitted at 35° to hydrogenation at one atmosphere using palladised charcoal. When these bromo compounds were refluxed with zinc and alcohol for 3 to 4 hours, a product, m. p. 184°, was obtained in each case which gave no depression of m. p. when mixed with ψ-santonin.

Monobromo-ψ-santonin oxime crystallised from dilute alcohol as colourless plates, m. p. 251° (decomp.) (Found: C 50·4; H, 5·4. $C_{15}H_{20}O_4NBr$ requires C, 50·3; H, 5·6%). Attempts to obtain the oxime of the tribromo compound were unsuccessful.

ψ-Santonin (0·1058 g.), titrated by Winkler's method (*loc. cit.*), required 15·84 c.c. 0·1004N-sodium bromate, equivalent to 0·127 g. bromine (four atoms of bromine = 0·127 g.). Similarly, 0·0684 g. dihydro-ψ-santonin required 10·06 c.c. 0·1004N-sodium bromate, equivalent to 0·081 g. bromine (four atoms of bromine = 0·082 g.).

Action of Mineral Acids on ψ-Santonin.—(a) *Sulphuric acid* (55%). Finely powdered ψ-santonin (0·25 g.) was introduced with stirring into a mixture of conc. sulphuric acid (2·5 c.c.) and water (3·7 c.c.), and the mixture was warmed

to 48—55° for 24 hours. After a short time the ψ-santonin passed into solution with the production of a bright red colour and shortly afterwards a crystalline solid was deposited. This was crystallised twice from 80% alcohol, when *desmotropo-ψ-santonin* was deposited as colourless needles (0·06 g.), m. p. 185—186°, $[\alpha]_D^{20°}$ + 67·9° (*c*, 2·461 in chloroform) (Found: 73·2, 73·3; H, 7·4, 7·3. $C_{15}H_{18}O_3$ requires C, 73·2; H, 7·3%). It was soluble in sodium hydroxide, insoluble in sodium carbonate, gave a red coloration with neutral ferric chloride and a deep pink nitroso compound. It gave a dull red coloration with *p*-nitrobenzenediazonium chloride. The *benzoate* prepared in alkaline solution crystallised from dilute alcohol as long needles, m. p. 164° (Found: C, 74·8; H, 6·2. $C_{22}H_{22}O_4$ requires C, 75·4; H, 6·3%). The *acetate* crystallised from dilute alcohol as colourless plates, m. p. 233° (Found: C, 70·5; H, 6·8. $C_{17}H_{20}O_4$ requires C, 70·8; H, 6·9%). This compound was not readily hydrolysed, but hydrolysis was effected by the use of concentrated methanolic potash when desmotropo-ψ-santonin was regenerated. This resistance to hydrolysis is characteristic of phenyl esters. The *methyl ether*, prepared by using methyl sulphate in alkaline solution, crystallised from dilute alcohol in tufts of silvery needles, m. p. 159—160° (Found: C, 73·3; H, 7·4. $C_{16}H_{20}O_3$ requires C, 73·8; H, 7·7%). Thionyl chloride had no action on desmotropo-ψ-santonin. Attempts to reduce the desmotropo compound by palladised charcoal were unsuccessful.

From the mother liquors obtained during the crystallisation of the desmotropo compound, an amorphous solid was obtained from which a crystalline *acetate* (needles, m. p. 239°) was obtained in small quantity. This compound has not yet been identified (Found: C, 71·4; H, 7·1. $C_{17}H_{20}O_4$ requires C, 70·8; H, 6·9%).

(b) *Formic acid.* The desmotropo compound was also obtained by refluxing ψ-santonin (0·5 g.) with formic acid (4 c.c.; 98%) for 2 hours. Excess formic acid was removed under reduced pressure and the residue was crystallised from alcohol as colourless plates (0·2 g.), m. p. and mixed m. p. 186°.

(c) *Concentrated hydrochloric acid.* Powdered ψ-santonin (1 g.) was stirred into conc. hydrochloric acid (5 g.). The solution quickly became yellow, and in a short time a crystalline solid was deposited. After 1 hour, this was collected, washed with a little concentrated hydrochloric acid and then with water, leaving a colourless crystalline solid (0·7 g.), m. p. 172—173°. It was crystallised twice from dilute acetic acid as fine colourless needles, m. p. 175—176°, $[\alpha]_D^{20°}$ + 25·2° (*c* 1·8 in chloroform), readily soluble in sodium carbonate with effervescence and recovered on acidification (Found: C, 63·9; H, 7·5; *M*, 286. $C_{15}H_{22}O_5$ requires C, 63·8; H, 7·8%; *M*, 282). Oximation in alcohol using sodium acetate gave a nitrogenous compound which was readily soluble in water and contained sodium. By crystallisation from the minimum quantity of water, it was obtained in clusters of needles which darkened at 200° and did not melt below 400° (Found: N, 4·3. $C_{15}H_{22}O_5NNa$ requires N, 4·4%). Attempts to acetylate the compound m. p. 175—176° gave inconclusive results, but on treatment with 55% sulphuric acid it gave desmotropo-ψ-santonin.

Dihydro-ψ-santonin and its anhydro compound were both unaltered by conc. hydrochloric acid and 55% sulphuric acid.

Attempted dehydrogenation of the desmotropo compound by selenium failed, since the compound sublimed too readily. Dehydrogenation was effected by heating gradually and with stirring a solution of the desmotropo compound (0·5 g.) in potassium hydroxide (0·5 g.) and water (2 c.c.). Fusion commenced at 220° and gas evolution took place at 240°. The temperature was then raised gradually to 310—320° and kept there for about 10 minutes, until gas evolution had ceased. The cooled melt was extracted with water and the violet solution shaken with a little charcoal and filtered. The filtrate was acidified and on steam-distillation a colourless crystalline solid (0·15 g.), m. p. 76—78°, was obtained. It was crystallised thrice from ligroin as colourless needles, m. p. 81—82°. It was found impossible to raise the m. p. above this value, but the product did not depress the m. p. of authentic 2:4-dimethyl-1-naphthol (Cornforth, Cornforth, and Robinson, *loc. cit.*, give m. p. 84—85°) (Found: C, 83·4; H, 7·1. Calc. for $C_{12}H_{12}O$: C, 83·7; H, 7·0%). Its *carbanilate* crystallised from ligroin (80/100°) as clusters of colourless needles, m. p. 174—175°. The m. p. when mixed with the carbanilate prepared from 2:4-dimethyl-1-naphthol, obtained according to Cornforth, Cornforth, and Robinson, showed no depression (Found: C, 78·0; H, 6·3. $C_{16}H_{17}O_2N$ requires C, 78·4; H, 5·8%). Its picrate crystallised from aqueous alcohol as deep red needles giving m. p. and mixed m. p. with authentic material 143—144° (Found: C, 54·2; H, 3·8. Calc. for $C_{12}H_{12}O,C_6H_3O_7N_3$: C, 53·9; H, 3·7%).

Clemmensen reduction of dihydro-ψ-santonin. The dihydro compound (0·4 g.), amalgamated zinc (4 g.) and concentrated hydrochloric acid (7 c.c.) were refluxed for 18 hours; then a further quantity of the acid (3 c.c.) was added and the boiling continued for 8 hours. After cooling, the odoriferous oil was extracted with ether, dried over sodium sulphate and the ether removed. As the resulting colourless gum (0·07 g., b. p. 140°/1 mm.) showed no signs of crystallisation after standing for a fortnight, it was subjected to selenium dehydrogenation. The product from several such experiments (1·55 g.) was heated with selenium (4 g.) at 280—340° for 48 hours and finally at 340—350° for a further 12 hours. The residue was extracted with ligroin (b. p. 60—80°) and the solvent removed. The residue was distilled from sodium giving an oil (0·25 g., b. p. 80°/1 mm.). This residue (0·15 g.) in alcohol was treated with picric acid (0·18 g.) in alcohol and the orange prisms collected. On crystallisation from alcohol the picrate was obtained as long, orange needles, m. p. 96°. The m. p. was not depressed on admixture with the picrate of 1-methyl-7-ethylnaphthalene (Harvey, Heilbron, and Wilkinson, *J.*, 1930, 423).

Ozonolysis experiments. A number of experiments were performed in which ψ-santonin (1 g.) dissolved in purified chloroform (20 c.c.) was submitted to the action of 6% ozonised oxygen for periods of 6 to 9 hours at 0—5°. The solvent was removed and the syrupy residue was steam distilled into an aqueous alcoholic solution of "dimedon," from which the formaldehyde condensation product (0·06 g.), m. p. 190° (cp. Vorlander, *Z. anal. Chem.*, 1929, **74**, 241) was obtained. The residue, remaining after steam distillation, was an intractable syrup.

Efforts to convert desmotropo-ψ-santonin to a ψ-santonous acid were unsuccessful. Sodium amalgam, hydriodic acid and red phosphorus, and zinc and acetic acid were employed, but the compound was either recovered unchanged or it gave an intractable syrup.

All attempts to dehydrate ψ-santonin were fruitless. It distilled unchanged from anhydrous sodium sulphate, copper sulphate and calcium oxide.

Some Experiments on the Opening of Lactone Rings with Hydroxylamine.—(i) *Action of hydroxylamine on* p-*toluenesulphonyl*-6:6-*dimethyl*-2-*morpholone.* This compound (0·5 g.) in alcohol (5 c.c.) was refluxed for 1 hour with hydroxylamine hydrochloride (0·5 g.) and anhydrous sodium acetate (1·8 g.). Alcohol was distilled away and the residue was washed with water and crystallised from alcohol. Two crops of crystals were obtained. The first had m. p. 132° and was identical with the starting material, the second was crystallised twice from dilute alcohol as long, colourless prisms, m. p. 105° (decomp.). It was readily soluble in sodium hydroxide and gave a blood-red coloration with neutral ferric chloride, and a sparingly soluble copper salt with ammoniacal copper sulphate. Its properties, generally, conformed with those expected of N-p-*toluenesulphonyl*-N-β-*hydroxyisobutylacethydroxamic acid* (Found: C, 48·9; H, 6·4. $C_{13}H_{20}O_5N_2S$ requires C, 49·4; H, 6·3%).

(ii) *Action of hydroxylamine on coumarin.* Coumarin (0·5 g.), hydroxylamine hydrochloride (0·4 g.), sodium acetate (0·5 g.) and alcohol (5 c.c.) were refluxed for 2 hours. The product was isolated as in (i) and crystallised twice from alcohol when β-2-*hydroxyphenylacrylhydroxamic acid* was obtained as colourless prisms (0·1 g.), m. p. 252° (decomp.) (Found: C, 60·4; H, 5·2. $C_9H_9O_3N$ requires C, 60·3; H, 5·0%).

(iii) *Action of hydroxylamine on the lactone of* cyclo*hexanol-2-β-propionic acid* (Cook and Lawrence, *J.*, 1937, 823). From this lactone (2 g.) a very small quantity of a very hygroscopic nitrogenous material was obtained which, on crystallisation from alcohol and ether, was obtained as colourless plates, m. p. 115—116°. There was insufficient material for analysis.

(iv) *Lactone of* cyclo*hexanol-2-α-propionic acid.* Ethyl *cyclo*hexanone-2-carboxylate (40 g.), ethyl α-bromopropionate (42 g.) and sodium ethoxide (from 5·4 g. sodium and 120 c.c. alcohol) were refluxed overnight. The alcohol was removed and the residue extracted with ether and fractionated, giving *ethyl* cyclo*hexanone-2-carboxylate-2-α-propionate* (25 g.) as a colourless oil, b. p. 158—163°/6—8 mm. (Found: C, 62·6; H, 8·0. $C_{14}H_{22}O_5$ requires C, 62·2; H, 8·1%). Attempts to hydrolyse this compound with hydrochloric acid (compare Robinson and Openshaw, *J.*, 1937, 944) gave poor results, but hydrolysis with baryta gave somewhat higher yields than with aqueous methanolic potassium hydroxide (compare Haworth and Mavin, *J.*, 1933, 1015). The ester (25 g.) was added to barium hydroxide (50 g. of monohydrate) in a mixture of methanol (250 c.c.) and water (250 c.c.) and the whole heated with shaking for 2 hours. Methanol was distilled away and the residue acidified and extracted with ether; the extract was dried with sodium sulphate and fractionated. Two fractions were obtained: (*a*) 2 g., b. p. 94—96°/0·25 mm., (*b*) 6 g., b. p. 153—156 (0·25 mm.). Fraction (*b*) solidified on cooling and was crystallised from ligroin as rosettes of needles, m. p. 135° (Found: C, 63·61, H, 8·4. $C_9H_{14}O_3$ requires C, 63·5; H, 8·2%). This was the required cyclo*hexanone-2-α-propionic acid.* Its 2 : 4-*dinitrophenylhydrazone* crystallised from alcohol as orange needles, m. p. 244° (Found: C, 51·7; H, 5·2. $C_{15}H_{18}O_6N_4$ requires C, 51·4; H, 5·1%), and its *semicarbazone* from water as prisms, m. p. 185—186° (decomp.) (Found: C, 51·1; H, 7·5. $(C_{10}H_{17}O_3N_3)_2H_2O$ requires C, 50·8; H, 7·6%).

Reduction of the above acid. The acid (1·7 g.) in alcohol (50 c.c.) was refluxed with sodium (3 g.) until all the sodium had dissolved. Alcohol was removed, water was added and the mixture was acidified and extracted with ether. The extract was fractionated and a colourless liquid (1 g.), b. p. 106—108/0·5 mm., was collected. This was the required *lactone* (Found: C, 69·7; H, 9·0. $C_9H_{14}O_2$ requires C, 70·1; H, 9·1%). All attempts to obtain a nitrogen containing compound from this lactone by treatment with hydroxylamine failed, as did all attempts at hydrogenolysis using palladised charcoal.

Fraction (*a*), b. p. 94—96/0·25 mm., dissolved slowly in sodium hydroxide, readily decolorised bromine water and gave a 2 : 4-*dinitrophenylhydrazone* which crystallised from alcohol as golden-yellow plates, m. p. 154°, insoluble in sodium carbonate (Found: C, 51·3, 51·8; H, 5·5, 4·9. $C_{15}H_{18}O_6N_4$ requires C, 51·4; H, 5·1%). This compound was not investigated further.

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KING'S COLLEGE, UNIVERSITY OF DURHAM, NEWCASTLE-UPON-TYNE. [*Received, July 31st*, 1945.]

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12. *The Constitution of ψ-Santonin. Part II. The Preparation of Certain Dimethyl Naphthols.*

By WESLEY COCKER.

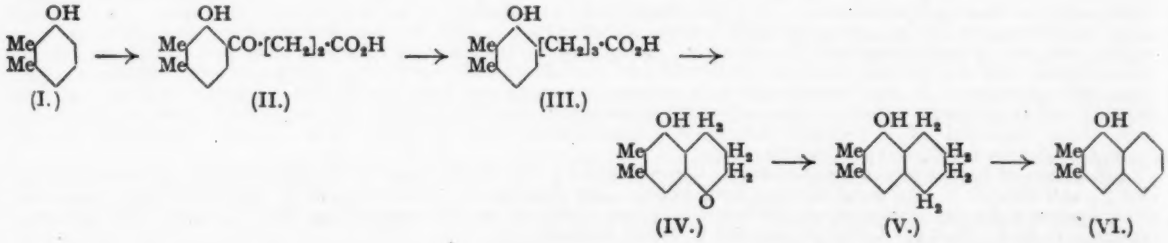
The preparations of 1 : 3-dimethyl-2-naphthol, 3 : 4-dimethyl-2-naphthol, and 2 : 3-dimethyl-1-naphthol are now described.

DEGRADATION of desmotropo-ψ-santonin by fusion with potassium hydroxide gave a dimethyl naphthol (Clemo and Cocker, this vol., p. 32) which, by analogy with the degradation product of *l*-santonin, was expected to be a dimethyl-β-naphthol with all substituents in the same ring. Only one of the three possible dimethyl-β-naphthols of this type had been described, namely 1 : 4-dimethyl-2-naphthol (Cannizzaro and Carnelutti, *Ber.*, 1879, **12**, 1575; 1880, **13**, 1516), obtained from *l*-santonin, and therefore 1 : 3-*dimethyl-2-naphthol* and 3 : 4-*dimethyl-2-naphthol* have been prepared. None of these naphthols was identical with that obtained from desmotropo-ψ-santonin, but it was later shown (Clemo and Cocker, *loc. cit.*) that the latter was identical with 2 : 4-dimethyl-1-naphthol (Cornforth, Cornforth, and Robinson, *J.*, 1943, 168).

3 : 4-Dimethyl-1-naphthol was previously known (Kruber and Schade, *Ber.*, 1935, **68**, 11), and in order to complete our knowledge of the six possible dimethyl naphthols with all the substituents in the same ring, 2 : 3-*dimethyl-1-naphthol* has also been prepared.

The general method of preparation has been the condensation of succinic anhydride with the appropriate xylyl methyl ether followed by Clemmensen reduction, ring closure, further reduction of the cyclic ketone, and dehydrogenation.

In general, the condensation with succinic anhydride takes place *para* to the methoxy group, and this gives the desired keto acid in the preparation of 1 : 3-dimethyl-2-naphthol and 3 : 4-dimethyl-2-naphthol. In the preparation of 2 : 3-dimethyl-1-naphthol according to the following scheme it is necessary to obtain an *ortho*-hydroxy-keto acid (II).

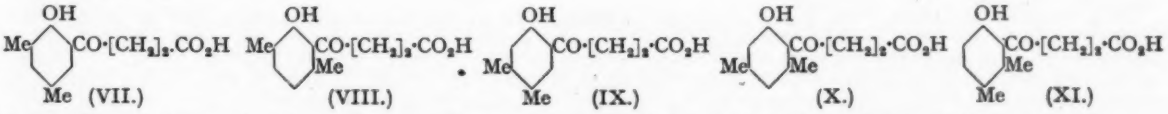


(I.) (II.) (III.) (IV.) (V.) (VI.)

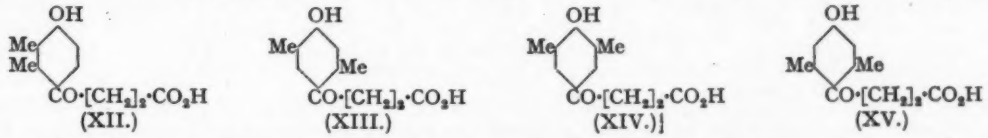
Compound (II) is obtained by making use of the fact that in the Fries rearrangement of phenolic esters the acyl group usually migrates to the *ortho* position when the reaction with aluminium chloride is performed at temperatures of 130—140° (compare Eykmann, *Chem. Weekblad*, 1904, **1**, 453; Rosenmund and Schnurr, *Annalen*, 1928, **460**, 56). One objection to this method is that aluminium chloride frequently causes the migration of methyl groups (compare Auwers, *Annalen*, 1928, **460**, 254; Baddeley, *J.*, 1943, 273, 527), but there is no evidence of this happening in the present instance.

The *o*-xylyl 3-hydrogen succinate readily dissociates on warming, and it is necessary to effect the rearrangement by the reversal of the usual method of adding the aluminium chloride to the heated ester. Consequently, reduced yields are obtained if attempts are made to use more than about 2 g. of ester at a time, but, with this quantity, an acid, concluded to be (II) for reasons stated below, is obtained in 60% yield. It couples with diazotised *p*-nitroaniline.

If migration of methyl groups took place during the Fries rearrangement, one of the following compounds could be produced :



In addition, if the succinoyl group migrated to the *para* position one of the following would be expected :



Compounds (VII) and (XIV) may be excluded, since, under ordinary conditions, these would not couple with diazotised *p*-nitroaniline. Also compounds (VIII), (X), (XI), and (XV) would be unlikely to undergo cyclisation after reduction without loss of a methyl group. Of the remaining possibilities, compounds (IX), (XII), and (XIII) would ultimately lead, respectively, to 3 : 4-dimethyl-1-naphthol, 3 : 4-dimethyl-2-naphthol and 1 : 4-dimethyl-2-naphthol, all of which are different from the dimethyl naphthol obtained. The keto acid, obtained by the Fries rearrangement, could therefore only be (II).

The conversion of the acid (III) to the cyclic *ketone* (IV) by concentrated sulphuric acid at 60° gives very poor yields due to sulphonation, only to be expected of a xylenol having an unsubstituted *para* position to the hydroxy group. The cyclisation is, however, efficiently performed by the use of 80% sulphuric acid at the water-bath temperature. From the above evidence and the fact that the dimethyl naphthol obtained from (IV) couples with diazotised *p*-nitroaniline to give an azo dye, it is concluded that compound (VI) has the structure indicated.

Attempts to nitrate 6 : 7-dimethyl-1 : 2 : 3 : 4-tetrahydronaphthalene so as to afford a more direct method to 2 : 3-dimethyl-1-naphthol were discouraging. Nitration in acetic anhydride gave an oil having a constant boiling point, but it was obviously a mixture of a nitro compound and the original dimethyl tetralin, since reduction gave only a trace of amine, presumably 5-amino-6 : 7-dimethyl-1 : 2 : 3 : 4-tetrahydronaphthalene mixed with the original dimethyl tetralin. Nitration in sulphuric acid gave a charred mass from which a very small quantity of a dinitro compound, presumably 5 : 8-dinitro-6 : 7-dimethyl-1 : 2 : 3 : 4-tetrahydronaphthalene, was isolated. The method was therefore abandoned.

Experimental.

1 : 3-*Dimethyl*-2-*naphthol*.—*β*-(4-*Methoxy*-3 : 5-*dimethyl*)*benzoylpropionic acid*. Technical 1 : 3 : 2-xylenol (2 : 6-dimethylphenol) was distilled in a vacuum and collected at 92°/17 mm. It had m. p. 44—45° (Noelting, *Ber.*, 1888, **21**, 2829, gives m. p. 47—48°), but it was considered to be pure enough for further work. It was methylated by methyl sulphate in sodium hydroxide and the methyl ether collected at 180—183°.

A mixture of 1 : 3 : 2-xylyl methyl ether (13·4 g.), succinic anhydride (10 g.), and dry benzene (25 c.c.) at 10° was stirred vigorously and treated with finely powdered aluminium chloride (13·4 g.). The mixture was then shaken for 24 hours, decomposed with ice and hydrochloric acid and the crystalline solid was collected. It was washed with dilute hydrochloric acid, then with water and freed from residual benzene. It was dissolved in cold 10% sodium carbonate solution, filtered (charcoal) and reprecipitated with hydrochloric acid. The precipitate after washing and drying weighed 8·2 g., m. p. 112°. This was sufficiently pure for the subsequent stages of the reaction. When crystallised from a large volume of hot water it yielded colourless prisms, m. p. 114—115° (Found : C, 66·2; H, 7·0. $C_{13}H_{16}O_4$ requires C, 66·1; H, 6·8%). The p-*nitrobenzylthiouronium salt* crystallised from 50% alcohol as silvery needles, m. p. 142° (Found : C, 54·8; H, 6·0. $C_{21}H_{25}O_6N_3S,H_2O$ requires C, 54·2; H, 5·8%).

γ-(4-*Methoxy*-3 : 5-*dimethyl*)-*phenylbutyric acid*. A mixture of the above keto acid (5·8 g.), amalgamated zinc (40 g.), hydrochloric acid (60 c.c.), and water (10 c.c.) was refluxed for 18 hours, cooled, and extracted with ether. After removal of the solvent, the residue was shaken with dimethyl sulphate (5 c.c.) and sodium hydroxide and then acidified. The oil quickly solidified; it was washed with water and dried yielding 5·0 g. of the required material, m. p. 65—66°, sufficiently pure for the next stage. When crystallised from ligroin, it was obtained as colourless prisms, m. p. 72° (Found : C, 70·3; H, 8·2. $C_{13}H_{18}O_3$ requires C, 70·3; H, 8·1%). Its p-*nitrobenzylthiouronium salt* crystallised from dilute alcohol as colourless needles, m. p. 131—132° (Found : C, 58·3; H, 6·1. $C_{21}H_{27}O_5N_3S$ requires C, 58·2, H, 6·2%).

1-*Keto*-7-*methoxy*-6 : 8-*dimethyl*-1 : 2 : 3 : 4-*tetrahydronaphthalene*. The above butyric acid (3 g.) was stirred into concentrated sulphuric acid (15 c.c.) and the mixture maintained at 65—70° for 10 minutes. When cold, it was poured

on to ice and extracted with chloroform. The extract was washed thrice with 5% sodium carbonate, dried and fractionated. The required *ketone* (1·7 g.) was collected at 141—142°/1 mm. (Found: C, 76·3; H, 7·9. $C_{13}H_{16}O_2$ requires C, 76·5; H, 7·8%). The compound solidified and was crystallised from ligroin as colourless plates, m. p. 40°. Its 2 : 4-*dinitrophenylhydrazone* crystallised from benzene as orange needles with a violet reflex, m. p. 246—247° (decomp.) (Found: C, 59·2; H, 5·25. $C_{19}H_{20}O_5N_4$ requires C, 59·4; H, 5·2%).

7-*Methoxy*-6 : 8-*dimethyl*-1 : 2 : 3 : 4-*tetrahydronaphthalene*. The above ketone (5 g.) was reduced during 14 hours with a mixture of conc. hydrochloric acid (40 c.c.), water (10 c.c.), alcohol (70 c.c.), and amalgamated zinc (40 g.). Alcohol was removed and the residue shaken with dimethyl sulphate (5 c.c.) and 2N-sodium hydroxide, cooled and extracted with ether. The extract was dried, fractionated, and the *compound* collected (3·5 g.), at 109°/0·2 mm. (Found: C, 81·9; H, 10·0. $C_{13}H_{18}O$ requires C, 82·1; H, 9·5%).

7-*Hydroxy*-6 : 8-*dimethyl*-1 : 2 : 3 : 4-*tetrahydronaphthalene*. The above methyl ether (3·7 g.) was gently refluxed with hydriodic acid (*d* 1·7, 15 c.c.) for 90 minutes. The mixture was cooled, the solid separated and washed first with dilute sodium bisulphite, then with water and dried, yielding 3·3 g. of the required *compound*, m. p. 91—92°. It was crystallised from dilute alcohol as long, colourless needles, m. p. 97·5—98° (Found: C, 81·9; H, 9·1. $C_{12}H_{16}O$ requires C, 81·8; H, 9·1%). It was sparingly soluble in dilute sodium hydroxide, but dissolved in 20% sodium hydroxide. Its *carbanilate* crystallised from aqueous alcohol as colourless prisms, m. p. 181·5—182·5° (Found: C, 77·0; H, 7·1. $C_{19}H_{21}O_2N$ requires C, 77·3; H, 7·1%).

1 : 3-*Dimethyl*-2-*naphthol*. The above tetrahydro compound (0·2 g.) was heated with selenium (0·5 g.) at 330—340° for 2—3 hours. The cooled product was extracted with methyl alcohol, distilled in steam, and crystallised from dilute alcohol as felted needles (0·12 g.), m. p. 89—90° (Found: C, 83·5; H, 7·1. $C_{12}H_{12}O$ requires C, 83·7; H, 7·0%). Its *picrate* crystallised from ligroin (b. p. 80—100°) as scarlet needles, m. p. 132—133° (Found: C, 54·0; H, 4·0. $C_{12}H_{12}O,C_6H_3O_7N_3$ requires C, 53·9; H, 3·7%). Its p-*toluenesulphonate* crystallised from ligroin as colourless prisms, m. p. 85—86° (Found: C, 69·6; H, 5·6. $C_{19}H_{18}O_3S$ requires C, 69·9; H, 5·5%). Its *carbanilate* crystallised from alcohol as silvery plates, m. p. 197° (Found: C, 77·9; H, 5·9. $C_{19}H_{17}O_2N$ requires C, 78·3; H, 5·9%).

3 : 4-*Dimethyl*-2-*naphthol*.—o-3-*Xylenol*. Technical *o*-xylene (50 g.) was nitrated as described by Emerson and Smith (*J. Amer. Chem. Soc.*, 1940, **62**, 141), the product was first steam distilled, then fractionated, the fraction, b. p. 130—140°/30 mm., being collected. This was again fractionated and collected (60—62 g.) at 127—130°/15 mm. The product, consisting largely of 3-nitro-*o*-xylene, was then reduced in methanol (60 c.c.) with Raney nickel (1 g.) at 100—110°/100 atm., yielding *o*-3-xylidine (43 g.), b. p. 222—224°.

The method of purification suggested by Emerson and Smith (*loc. cit.*) making use of a difference in solubility of the sulphates of the *o*-3- and *o*-4-xylidines was rejected in favour of a purification through the acetyl derivatives, but in the later experiments it was found that the purification could best be performed after diazotisation. Diazotisation was carried out in the following manner. The above xylidine mixture (66 g.) in dilute hydrochloric acid (190 c.c. concentrated acid, 190 c.c. water) and finely powdered ice (500 g.) was cooled to −10° and sodium nitrite (41·3 g.) dissolved in the minimum quantity of water slowly added. Diazotisation was completed by further stirring for 30 minutes at 0° to −10°. This solution was then added to a boiling solution of copper sulphate (12 g.) in 50% sulphuric acid (55 c.c.), the xylenol being removed by steam as it was produced. The semi-solid mass collected from the distillate was distilled and collected at 212—224°. The distillate solidified, was pressed on porous plate, and crystallised from ligroin as colourless plates (12 g.), m. p. 72°.

β-4-*Methoxy*-2 : 3-*dimethylbenzoylpropionic acid*. *o*-Xylenol-3-methyl ether (6·7 g.) was condensed with succinic anhydride (5 g.) in benzene (20 c.c.) with aluminium chloride (6·7 g.). The mixture was stirred for 6 hours at room temperature and the required product isolated as previously described. The yield of practically pure material was 5·8 g., m. p. 172—173°. When crystallised from alcohol it formed long prisms, m. p. 174° (Found: C, 66·05; H, 6·6. $C_{13}H_{16}O_4$ requires C, 66·1; H, 6·8%). Its p-*nitrobenzylthiouronium salt* crystallised from dilute alcohol as colourless needles, m. p. 153° (decomp.) (Found: C, 56·0; H, 5·6. $C_{21}H_{25}O_6N_3S$ requires C, 56·4; H, 5·6%).

γ-(4-*Methoxy*-2 : 3-*dimethyl*)-*phenylbutyric acid* was obtained (4·3 g.), m. p. 113—114°, by the Clemmensen reduction of the above keto acid (5 g.) with amalgamated zinc (40 g.) and concentrated hydrochloric acid (40 c.c.). It was not found necessary to remethylate the compound before isolation. A portion was crystallised from dilute alcohol as silvery plates, m. p. 119—120° (Found: C, 70·2; H, 7·8. $C_{12}H_{18}O_3$ requires C, 70·3; H, 8·1%).

Its p-*nitrobenzylthiouronium salt* crystallised from dilute alcohol as pale yellow prisms, m. p. 148—149° (decomp.) (Found: C, 58·6; H, 6·3. $C_{21}H_{27}O_5N_3S$ requires C, 58·2; H, 6·2%).

1-*Keto*-7-*methoxy*-5 : 6-*dimethyl*-1 : 2 : 3 : 4-*tetrahydronaphthalene*. The above butyric acid (8 g.) was treated in the usual way with conc. sulphuric acid (40 c.c.) yielding 5·2 g. of the required ketone, m. p. 77—78°. It crystallised from ligroin as colourless needles, m. p. 78—79° (Found: C, 76·2; H, 7·6. $C_{13}H_{16}O_2$ requires C, 76·5; H, 7·8%). Its *semicarbazone* crystallised from alcohol as needles, m. p. 258—259° (Found: C, 64·6; H, 7·3. $C_{14}H_{19}O_2N_3$ requires C, 64·4; H, 7·3%).

7-*Methoxy*-5 : 6-*dimethyl*-1 : 2 : 3 : 4-*tetrahydronaphthalene* was prepared by the Clemmensen reduction of the above ketone (6 g.) yielding colourless needles (5 g.), m. p. 65°, after purification by sublimation under reduced pressure (Found: C, 82·7; H, 9·4. $C_{13}H_{18}O$ requires C, 82·1; H, 9·5%).

7-*Hydroxy*-5 : 6-*dimethyl*-1 : 2 : 3 : 4-*tetrahydronaphthalene*, purified by sublimation, consisted of long prisms, m. p. 114—115° (Found: C, 81·2; H, 8·8. $C_{12}H_{16}O$ requires C, 81·8; H, 9·1%). Its *carbanilate* crystallised from alcohol as needles, m. p. 174—175° (Found: C, 77·0; H, 7·1. $C_{19}H_{21}O_2N$ requires C, 77·3; H, 7·1%). Its p-*toluenesulphonate* crystallised from ligroin as needles, m. p. 108—109° (Found: C, 69·0; H, 6·5. $C_{19}H_{22}O_3S$ requires C, 69·1; H, 6·7%).

3 : 4-*Dimethyl*-2-*naphthol*. The above tetrahydro compound (0·2 g.) was heated for 4 hours at 330—340° with selenium (0·5 g.). The cooled product was distilled in steam, yielding a white solid which crystallised first from dilute alcohol and then from ligroin as long prisms (0·1 g.), m. p. 113°, and depressed on admixture with the tetrahydro compound (Found: C, 83·9; H, 7·0. $C_{12}H_{12}O$ requires C, 83·7; H, 7·0%). Its p-*toluenesulphonate* crystallised from ligroin as colourless needles, m. p. 128° (Found: C, 69·7; H, 5·6. $C_{19}H_{18}O_3S$ requires C, 69·9; H, 5·5%).

2 : 3-*Dimethyl*-1-*naphthol*.—*Nitration of* 6 : 7-*dimethyl*-1 : 2 : 3 : 4-*tetrahydronaphthalene*. This compound (Barnett and Sanders, *J.*, 1933, 435) (12 g.) in acetic anhydride (10 c.c.) was stirred at 0° to −5° and fuming nitric acid (*d* 1·515, 3·15 c.c.) in acetic anhydride (3 c.c.) was added. Considerable heat was developed if the addition was made too rapidly, and in order to keep the temperature within the prescribed limits the addition took 90 minutes, after which stirring was continued for 1 hour. The mixture was poured on to ice, extracted with ether, the extract was washed with dilute sodium hydroxide and then fractionated. About 7 g. of the starting material was first collected and then a pale yellow liquid was collected at 140—153°/1 mm. This was redistilled and collected (6·9 g.) at 142—143°/1—2 mm. Although this liquid was fractionated several times, a pure mononitro compound was not obtained (Found: C, 76·2; H, 7·6. $C_{12}H_{15}O_3N$ requires C, 70·2; H, 7·3%). The mixture was reduced by iron powder in alcohol yielding 0·2 g. of the required 5-*amino*-6 : 7-*dimethyl*-1 : 2 : 3 : 4-*tetrahydronaphthalene*, b. p. 130°/1 mm. It was characterised as its *acetyl* compound, which crystallised from dilute alcohol as fine colourless needles, m. p. 201° (Found: C, 77·1; H, 8·9. $C_{14}H_{19}ON$ requires C,77·4; H, 8·8%). Its *chloroplatinate* crystallised from hot water as pale yellow prisms, m. p. 224—225°

(decomp.), but appeared to be hydrolysed on being heated in water (Found: C, 38·5; H, 4·8; Pt (as residue), 24·6. $C_{24}H_{28}N_2Cl_6Pt$ requires C, 37·9; H, 4·73; Pt, 25·65%).

Nitration in sulphuric acid. The dimethyltetralin (1 g.) stirred with concentrated sulphuric acid (5 g.) was cooled to −10° and slowly treated with a mixture of nitric acid (*d* 1·42, 0·5 g.) and concentrated sulphuric acid (3 c.c.). Stirring was continued for 15 minutes and the mixture was then poured into water (50 c.c.). The dark-green solid was collected, washed with sodium carbonate, then with water, and dried. It was extracted with alcohol (charcoal) from which a yellow crystalline compound was isolated. On crystallisation from benzene–ligroin it was deposited as colourless flat prisms (0·05 g.), m. p. 203° (Found: C, 57·8; H, 5·6. $C_{12}H_{14}O_4N_2$ requires C, 57·6; H, 5·6%).

β-(6-Hydroxy-4 : 5-dimethyl)-benzoylpropionic Acid.—o-Xylyl 3-hydrogen succinate. A mixture of *o*-3-xylenol (10 g.) and succinic anhydride (10 g.) was heated at 130° for half an hour and then cooled. The solid product was finely powdered, suspended in water (100 c.c.) and sodium carbonate added until just alkaline to phenolphthalein. The mixture was then diluted to 300 c.c.; excess *o*-3-xylenol (0·5—1·0 g.) then separated and was collected. The filtrate was treated with charcoal and again filtered and, on acidification, a colourless oil was produced. This solidified on scratching and was collected, washed, and dried in a desiccator yielding the required *ester* (12·7 g.), m. p. 67—69°. When crystallised from benzene–ligroin, it was obtained as colourless flat prisms, m. p. 72—73° depressed on admixture with the original xylenol (Found: C, 65·4; H, 6·5. $C_{12}H_{14}O_4$ requires C, 64·9; H, 6·3%). The ester readily dissociated on heating and was hydrolysed even on warming with dilute ammonia.

Fries rearrangement. The crude ester (1·0 g.) was slowly added with stirring to finely powdered aluminium chloride (1·0 g.) heated to 130°. The temperature was raised to 140° during 20 minutes and the mixture then cooled. It was finely powdered and added slowly to dilute hydrochloric acid and stirred until all lumps had disappeared. The product was collected, washed with dilute hydrochloric acid, then with water, and extracted with dilute sodium carbonate. From the extract after filtration the required acid was obtained by acidification. It was crystallised from dilute alcohol as long radiating needles (0·6 g.), m. p. 188—189° (Found: C, 64·9; H, 6·3. $C_{12}H_{14}O_4$ requires C, 64·9; H, 6·3%).

γ-(6-Hydroxy-4 : 5-dimethyl)-phenylbutyric acid. The above keto acid (4 g.) was reduced with amalgamated zinc (40 g.) and concentrated hydrochloric acid (40 c.c.) for 16 hours. The solid product was collected and crystallised from dilute alcohol as fine needles (2·5 g.), m. p. 109—110° (Found: C, 68·9; H, 7·55. $C_{12}H_{16}O_3$ requires C, 69·2; H, 7·7%).

8-Hydroxy-1-keto-6 : 7-dimethyl-1 : 2 : 3 : 4-tetrahydronaphthalene. The above butyric acid (2·5 g.) was cyclised by heating for 1½ hours on the water-bath with 80% sulphuric acid (25 c.c.) and the product was crystallised from ligroin as clusters of fern-like crystals (1·5 g.), m. p. 153—154°. (Found: C, 75·4; H, 7·2. $C_{12}H_{14}O_2$ requires C, 75·8; H, 7·4%). Its 2 : 4-*dinitrophenylhydrazone* crystallised from a large volume of alcohol as scarlet needles, m. p. 290° (Found: C, 58·2; H, 4·9. $C_{18}H_{18}O_5N_4$ requires C, 58·4; H, 4·9%). Its *acetate* crystallised from ligroin as colourless needles, m. p. 98° (Found: C, 72·1; H, 7·0. $C_{14}H_{16}O_3$ requires C, 72·4; H, 6·9%).

8-Hydroxy-6 : 7-dimethyl-1 : 2 : 3 : 4-tetrahydronaphthalene. The above ketone (4·5 g.) was reduced with amalgamated zinc (50 g.) and hydrochloric acid (100 c.c.) and the product crystallised from dilute alcohol in colourless needles (3·0 g.), m. p. 83·5° (Found: C, 82·1, H, 9·1. $C_{12}H_{16}O$ requires C, 81·8; H, 9·1%).

2 : 3-Dimethyl-1-naphthol. The tetrahydro compound (1·0 g.) was heated with selenium (3 g.) for 4 hours at 330—340° and then the mixture was distilled in steam yielding the required naphthol (0·3 g.), m. p. 77—78°. It was crystallised twice from dilute alcohol and obtained as rosettes of colourless needles, m. p. 84°, depressed on admixture with the tetrahydro compound and also on admixture with 2 : 4-dimethyl-1-naphthol, which has m. p. 84—85° (Found: C, 84·0; H, 7·1. $C_{12}H_{12}O$ requires C, 83·7; H, 7·0%). Its *picrate* crystallised from benzene–ligroin as scarlet needles, m. p. 143—144°, depressed on admixture with the picrate of 2 : 4-dimethyl-1-naphthol, which has m. p. 143—144° (Cornforth, Cornforth, and Robinson, *loc. cit.*) (Found: C, 54·3; H, 3·9. $C_{12}H_{12}O,C_6H_3O_7N_3$ requires C, 53·9; H, 3·7%). The new naphthol readily coupled with diazotised *p*-nitroaniline giving a deep red azo dye which was crystallised from dilute acetic acid as small deep ruby needles, m. p. 225—226° (decomp.) (Found: C, 67·0; H, 4·7. $C_{18}H_{15}O_3N_3$ requires C, 67·3; H, 4·7%).

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KING'S COLLEGE, UNIVERSITY OF DURHAM, NEWCASTLE-UPON-TYNE. [*Received, July 31st*, 1945.]

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13. *Researches on Acetylenic Compounds. Part I. The Preparation of Acetylenic Ketones by Oxidation of Acetylenic Carbinols and Glycols.*

By KENNETH BOWDEN, I. M. HEILBRON, E. R. H. JONES and B. C. L. WEEDON.

A new and convenient route to acetylenic ketones has been devised, consisting of chromic acid oxidation of the corresponding secondary alcohols, best in acetone solution, and simple ethynyl ketones (–CO·C≡CH), hitherto practically unknown, have now become readily available. In the various cases examined, which include the ethylenic acetylenyl-carbinol, propenylethynylcarbinol, the yields range from 40—80%, the ease of oxidation of the alcohols [R·CH(OH)·C≡C–] being in the order R = Ph, CH_2·CH:CH > Pr > Me. Both vinylacetylenyl and acetylenylvinyl ketones can also be produced by this means, but because of their instability low yields are obtained and, where possible, preparation by means of the vinylacetylenic Grignard reagents is preferable.

The acetylenic hydrogen of the ethynyl ketones is markedly acidic and although the ketones show no appreciable tendency to polymerise they undergo a variety of addition reactions with considerable facility. These additions have been investigated in detail and some of the results are described in the following papers. A study of the light absorption properties of a number of αβ-acetylenic ketones and of their 2 : 4-dinitrophenylhydrazones reveals essential similarities to the ethylenic analogues.

The acetylenic di-secondary glycols from crotonaldehyde and benzaldehyde are smoothly oxidised to the diketones, but the glycol from butaldehyde gives mainly the keto-alcohol (XII), the further oxidation to the diketone being much more difficult.

ONLY one example of an αβ-ethynyl * ketone (–CO·C≡CH) has as yet been described in the literature and although many routes to αβ-acetylenic keto-compounds of the type, R·CO·C≡CR′ (I) (R′ = alkyl or aryl) are known, comparatively few are of general applicability.

* The term " ethynyl " is applied to the group –C≡CH, containing one active hydrogen atom.

The method most frequently employed consists of treatment of alkali metal acetylides with acid bromides (the chlorides are frequently less effective) or anhydrides in inert media such as benzene or ether (*inter alia*, André, *Ann. Chim.*, **1913**, **29**, 557; Moureu and Brachin, *Bull. Soc. chim.*, **1904**, **31**, 345; **1906**, **33**, 134; **1907**, **35**, 1176; Nightingale and Wadsworth, *J. Amer. Chem. Soc.*, **1945**, **67**, 416), the process having been applied mainly to arylacetylenes. Both aryl- and alkyl-acetylenylmagnesium halides react with acetic anhydride or acetyl chloride giving acetylenic ketones (Kroeger and Nieuwland, *J. Amer. Chem. Soc.*, **1936**, **58**, 1861), the secondary reactions due to further condensation between the ketones and the Grignard reagents being said to be minimised by employing the acetylenylmagnesium chlorides and by carrying out the reactions at — 25°. Both the Grignard complexes and the alkali metal derivatives of acetylenes can be employed in condensations with esters, the formates yielding aldehydes (I; R = H), and other esters giving ketones, except when the acetylide is so basic as to bring about Claisen condensations with the esters (Moureu and Delange, *Bull. Soc. chim.*, **1902**, **27**, 375; **1904**, **31**, 1329).

Other applications of Grignard reagents to the preparation of acetylenic keto-compounds include their interaction with phenylpropiolic esters (Hurd and Cohen, *J. Amer. Chem. Soc.*, **1931**, **53**, 1072) and reactions between acetylenic Grignard complexes and α-chloro-ketones (Tiffeneau and Deux, *Compt. rend.*, **1941**, **213**, 753; **1942**, **214**, 892), when the primary products undergo a type of hydrobenzoin rearrangement on heating to 110°, giving either αβ- or βγ-acetylenic ketones depending upon the nature of the substituent groups present.

$$C_5H_{11}\cdot C{\equiv}C\cdot MgBr \xrightarrow{Et\cdot CO\cdot CH_2Cl} C_5H_{11}\cdot C{\equiv}C\cdot CEt(OMgBr)\cdot CH_2Cl \longrightarrow C_5H_{11}\cdot C{\equiv}C\cdot CO\cdot CH_2Et + MgBrCl$$

The partial hydration of conjugated diacetylenes (Grignard and Tchéoufaki, *Rec. trav. chim.*, **1929**, **48**, 901; Griner, *Ann. Chim.*, **1892**, **26**, 359) and Friedel–Crafts reactions with substituted propiolyl halides (Krafft and Heizmann, *Ber.*, **1900**, **33**, 3590; Simonis and Lear, *Ber.*, **1926**, **59**, 2908) have both been applied to the production of acetylenic ketones. The only example of the oxidation of an acetylenylcarbinol to the corresponding ketone, is that given by André (*Ann. Chim.*, **1913**, **29**, 564), although a number of instances of similar oxidations

$$Ph\cdot CH(OH)\cdot C{\equiv}C\cdot Ph \xrightarrow{CrO_3—AcOH} Ph\cdot CO\cdot C{\equiv}C\cdot Ph$$

of aromatic *bis*-secondary acetylenic glycols (Dupont, *Bull. Soc. chim.*, **1914**, **15**, 606) and of secondary diacetylenylcarbinols, $RC{\equiv}C\cdot CH(OH)\cdot C{\equiv}CR$ (Liang, *ibid.*, **1933**, **53**, 44; Chauvelier, *Compt. rend.*, **1941**, **212**, 793), are known.

The ready availability of the secondary acetylenyl-carbinols (II) and glycols suggested an investigation of their oxidation, especially of the aliphatic ethynylcarbinols, with chromic acid and good yields of ketones have been obtained in practically every case.

$$\text{(II.)}\quad R_1C{\equiv}C\cdot CH(OH)\cdot R \xrightarrow{CrO_3} R_1C{\equiv}C\cdot CO\cdot R \quad \text{(III.)}$$

The nature of the solvent employed, the concentrations of the reagents and the reaction temperature all have a marked influence on the reaction. The most satisfactory procedure consists in the addition of a solution of chromic anhydride in dilute sulphuric acid to an acetone solution of the carbinol; in some cases a sharp end-point is observed after the addition of the theoretical amount of the oxidising agent. Acetone is preferred as a solvent since the oxidations proceed at a far greater rate in this medium than in acetic acid. The most suitable conditions for the oxidation of any given carbinol are best determined by preliminary titration of small quantities (*ca.* 1 g.) with a standard chromic acid solution.

The reagent concentrations can usually be adjusted so that an upper layer, consisting mainly of an acetone solution of the ketonic product, separates during the course of the oxidation from the lower green (usually saturated) solution of chromium salts. The segregation of the product in this way appears to be of considerable importance in protecting it from further oxidation; the colour of this upper layer also gives a useful indication of the presence of any excess of chromic acid. When the ketone produced is itself readily oxidised, it is advisable to introduce the chromic acid solution well below the surface of the liquid, so as to avoid undue contact with the upper layer.

With readily oxidisable carbinols, satisfactory results can usually be obtained by using the theoretical quantity of oxidising agent but, in those cases where oxidation is slow, the use of an excess of chromic acid is desirable. The particular temperature employed, in the range 0—20°, depends upon the ease of oxidation of the carbinol; the temperature and the rate of addition of the chromic acid solution are mutually adjusted so that the reaction proceeds at a reasonable rate without any appreciable excess of oxidising agent ever being present in the reaction medium.

Oxidation of oct-3-yn-2-ol (IV) by this method gave, in 80% yield, the same oct-3-yn-2-one (V) as was

$$\underset{\text{(IV.)}}{Bu^nC{\equiv}C\cdot CH(OH)\cdot Me} \longrightarrow \underset{\text{(V.)}}{Bu^nC{\equiv}C\cdot CO\cdot Me} \xleftarrow{(Ac)_2O} Bu^nC{\equiv}CMgCl$$

obtained by the method of Kroeger and Nieuwland (*loc. cit.*) from 1-hexynylmagnesium chloride and acetic anhydride.

The only αβ-ethynyl ketone hitherto described in the literature is methyl ethynyl ketone, which was prepared by Petrov (*J. Gen. Chem. Russia*, **1940**, **10**, 1682) by acid hydrolysis of its enol methyl ether, the latter being obtained from butadiene by a multi-stage process. These ketones are now easily prepared by employing

the oxidation procedure described above and compounds of the type, R·CO·C:CH (VI), *viz.*, *phenyl ethynyl ketone* (VI; R = Ph) (80% yield), *propyl ethynyl ketone* (VI; R = Pr) (70%) and methyl ethynyl ketone (VI; R = Me) (40%) have been obtained in this way. In the latter case, because of the difficulty of separating the ketone from acetone, the reaction was carried out in water, with which methylethynylcarbinol is completely miscible.

Only a few rather complex examples of the ethylenic acetylenic ketones have so far been synthesised (Worrall, *J. Amer. Chem. Soc.*, 1938, **60**, 1266; Rossander and Marvel, *ibid.*, 1929, **51**, 934; cf. Nightingale and Wadsworth, *loc. cit.*). The oxidation method is again applicable for the preparation of such compounds and oxidations of propenylethynylcarbinol and its isomer, hex-3-en-5-yn-2-ol, have yielded *propenyl ethynyl ketone*, Me·CH:CH·CO·C:CH (VII) (75% yield), and *hex-3-en-5-yn-2-one*, Me·CO·CH:CH·C:CH (VIII), (50%). Only one example of the oxidation of a carbinol derived from a vinylacetylene has been investigated, and the ketone *5-methylhex-5-en-3-yn-2-one*, Me·CO·C:C·CR:CH_2 (IX; R = Me), was isolated only, however, in 10% yield, a large quantity of undistillable resin being formed. This was not surprising since the ketone has been found to be very unstable and appears to polymerise readily. The ketone synthesis involving the reaction of acetylenic Grignard reagents and acetic anhydride (Kroeger and Nieuwland, *loc. cit.*) has been reported to fail (see Nazarov and Elizarova, *Bull. Acad. Sci. U.R.S.S.*, 1940, 189) when applied to vinylacetylene. However, by addition of an ethereal suspension of methylvinylacetylenyl- or vinylacetylenyl-magnesium chloride to an excess of acetic anhydride at − 30°, the ketone (IX; R = Me) and the unsubstituted vinylacetylenyl ketone, *hex-5-en-3-yn-2-one* (IX; R = H), have been obtained in 25 and 16·5% yields respectively. On reversing the mode of addition, as originally advocated by Kroeger and Nieuwland, further condensation ensues between the ketone initially produced and the Grignard reagent and, from one experiment carried out in this way, only a 10% yield of (IX; R = Me) was obtained, the main product being the acetate of the tertiary carbinol, CH_2:CMe·C:C·CMe(OH)·C:C·CMe:CH_2 (X).

With certain exceptions, the acetylenic ketones described above are stable substances which can be kept indefinitely at 0° in the presence of a little quinol. In sharp contrast to the vinyl ketones, propyl ethynyl ketone was practically unaffected by heating with 1% of benzoyl peroxide for 48 hours at 100°. The vinyl acetylenic ketones (VIII and IX; R = Me) are not stable under the storage conditions mentioned above and with 1% of benzoyl peroxide at 20° during 48 hours, the ketone (IX; R = Me) was converted into a rubber-like polymer but its lower homologue (IX; R = H) did not polymerise appreciably on keeping.

The ketones containing the free ethynyl group possess marked lachrymatory and sternutatory properties. They readily form acetylides with ammoniacal cuprous and silver salts and they attack metallic copper with remarkable rapidity. The high reactivity of the ethynyl hydrogen atom is further evidenced by the fact that these ethynyl ketones quantitatively liberate methane from methylmagnesium iodide at ordinary temperatures, thus behaving analogously to compounds in which the ethynyl group is conjugated with an ethylenic linkage (Cymerman, Heilbron, and Jones, *J.*, 1945, 90); the mechanism of this activation is undoubtedly similar.

2 : 4-Dinitrophenylhydrazones were readily obtained from all of the ketones studied and, rather unexpectedly, these appear to be the normal derivatives, no cyclisation, such as has frequently been reported in reactions between acetylenic carbonyl compounds and hydrazine and its derivatives, having occurred. These derivatives show the expected light absorption properties and, in those cases where it would be anticipated, silver salts were readily formed. With semicarbazide acetate abnormal reactions ensue, phenyl ethynyl ketone, for example, giving a high melting product, probably the *di-semicarbazone* of *hydroxymethyleneacetophenone*, which has been formed by addition of semicarbazide to the acetylenic bond. The substituted ketone, oct-3-yn-2-one (V), gives a normal *semicarbazone* and a *phenylsemicarbazone*, the light absorption properties of the former being in good agreement with those of the semicarbazones of αβ-ethylenic carbonyl compounds (Evans and Gillam, *J.*, 1943, 565).

Dupont (*Bull. Soc. chim.*, 1914, **15**, 606), who effected the oxidation of several aromatic *bis*-secondary acetylenic glycols to the corresponding diketones with chromic acid in acetic acid, stated that the method was not applicable to aliphatic glycols, but gave no indication of the compounds examined or of the conditions employed. No aliphatic acetylenic diketones have been described in the literature, consequently the oxidation of several glycols by the method successfully developed for the carbinols has been investigated.

In view of the ease of oxidation of propenylethynylcarbinol, the corresponding glycol was examined first and, by using the theoretical quantity of chromium trioxide, a 40% yield of the *diketone* (XI) was obtained. The

(XI.) Me·CH:CH·CO·C:C·CO·CH:CH·Me Pr^a·CO·C:C·CH(OH)·Pr^a (XII.)

(XIII.) Pr^a·CO·C:C·CO·Pr^a Pr^a·C(:NDn)·CH:C(NHDn)·CO·Pr^a (XIV.)

[Dn = 2 : 4-$C_6H_3(NO_2)_2$·NH·]

behaviour of the glycol from butaldehyde under similar conditions was unexpected. The oxidation proceeded much more slowly than that of the crotonaldehyde glycol and there was a marked diminution in the oxidation rate after one-half of the chromic acid required to form the diketone (XIII) had been added. Taking advantage of this fact, the *keto-alcohol* (XII) has been obtained in 60% yield. Its Zerewitinoff value is one; it can be characterised through its dinitrophenylhydrazone and it exhibits light absorption (see table) similar to that of an αβ-acetylenic ketone. The highly reactive *diketone* (XIII) appears to be unstable and readily polymerises, but it has been isolated in poor yield as a pale yellow liquid by direct oxidation of the glycol; a better yield was obtained by oxidation of the keto-alcohol (XII). The *product*, obtained by allowing the

diketone to react with 2 : 4-dinitrophenylhydrazine, is probably best represented as (XIV). The two *keto-alcohols* (XV and XVI) have also been prepared in good yields by oxidation of the secondary–tertiary glycols.

(XV.) Me·CH:CH·CO·C:C·C(OH)Me_2 Me·CH:CH·CO·C:C·C(OH)Ph_2 (XVI.)

When the method described in this paper was applied to an aromatic acetylenic glycol, *viz.*, that from benzaldehyde, the oxidation proceeded rapidly and to completion, giving the diketone, dibenzoylacetylene, in 90% yield. In the various oxidations detailed above, it has invariably been observed that the acetylenic carbinols or glycols derived from aromatic or αβ-unsaturated aldehydes are much more readily oxidised than those from the saturated aldehydes. For carbinols or glycols of structure, R·CH(OH)·C:C–, the rate of oxidation for different values of R appears to be in the order Ph, CH_2·CH:CH > Pr > Me.

The ultra-violet light absorption properties of the various acetylenic ketones described above and of their 2 : 4-dinitrophenylhydrazones are listed in the table, together with comparative data which have been obtained for analogous ethylenic ketones. The locations of the maxima in the acetylenic and ethylenic series are practically identical, but as has already been noted for other conjugated systems containing acetylenic bonds (Jones and McCombie, *J.*, 1943, 261; Heilbron, Jones, and McCombie, J., 1944, 134; Heilbron, Jones, and Raphael, *J.*, 1944, 136), the molecular extinction coefficients of the acetylenic compounds are considerably lower than those of the corresponding ethylenic compounds. The lower intensity longer wave-length bands, usually observed with carbonyl compounds, are also exhibited by the acetylenic ketones. The general characteristics of the absorption of the dinitrophenylhydrazones are similar to those already recorded for ethylenic compounds (Braude and Jones, *J.*, 1945, 498) and the Δλ values, *i.e.*, differences between the locations of the main maxima of the derivatives and the parent ketones, are of the same order as for the ethylenic series.

In order to obtain the corresponding ethylenic compounds for spectrographic purposes, propyl and propenyl ethynyl ketones were semi-hydrogenated in the presence of a 0·3% palladium on barium sulphate catalyst. In both cases the reaction proceeded smoothly and by interrupting the experiments after one molar proportion of hydrogen had been absorbed it was possible to prevent any appreciable hydrogenation of the ethylenic linkages. The propyl vinyl ketone thus obtained was characterised by the preparation of the diethylamine and aniline adducts.

Light Absorption of Acetylenic Ketones and their 2 : 4-Dinitrophenylhydrazones.

(In alcohol except where stated otherwise.)

	Ketone.		2 : 4-Dinitrophenylhydrazone (main band only).		
	$\lambda_{max.}$ A.	$\epsilon_{max.}$	$\lambda_{max.}$ A.	$\epsilon_{max.}$	Δλ
Me·CO·C:CH	*ca.* 2150	5,000	3590	21,000	1440
			3650 *	25,500	
Pr·CO·C:CH	*ca.* 2140	4,500	3600	25,500	1460
			3655 *	26,500	
Me·CO·C:C·Bu	2180 ‖	7,500	3660	32,500	1455
Pr·CO·C:C·CH(OH)·Pr	2200	7,500	3640	26,000	1440
	2280 †	6,500			
Me·CO·CH:CH_2	2100 [1]	6,500	—	—	—
Pr·CO·CH:CH_2	<2220	>6,000	—	—	—
Me·CO·CH:CHMe [1]	2240	9,700	—	—	—
Ph·CO·C:CH	2645	14,500	—	—	—
	(2340) ‡	4,000			
Ph·CO·CH:CH_2 [5]	2475	10,500	—	—	—
Me·CH:CH·CO·C:CH	2230	8,500	3740	33,000	1410
	2430	7,000			
Me·CH:CH·CO·C:C·C(OH)Me_2	2380	13,500	3850 *	31,500	1470
	2510 †	11,500			
Me·CH:CH·CO·C:C·C(OH)Ph_2	2240	21,000	—	—	—
	2420—2510	16,500			
Me·CH:CH·CO·CH:CH_2	2280	9,500	—	—	—
	2360	9,500			
CMe_2:CH·CO·CH:CMe_2	2655 [2]	23,000	3950 * [3]	24,500	1295
Me·CO·CH:CH·C:CH	2550	11,500	3780 *	30,000	1230
Me·CO·C:C·CH:CH_2	2510	8,500	3670	26,000	1160
	2580 †	8,000	3770 *	27,500	
Me·CO·C:C·CMe:CH_2	2500—2620	9,000	3660	28,000	1100
			3770 *	26,000	
Me·CO·CH:CH·CH:CH·Me	2710 [4]	22,500	—	—	—
Pr·CO·C:C·CO·Pr	2200	4,000	—	—	—
	2290	4,000			
Ph·CO·C:C·CO·Ph	2210 §	14,000	—	—	—
	2690	23,500			
Me·CH:CH·CO·C:C·CO·CH:CH·Me	2420	20,500	—	—	—
	2450	20,500			
Me·CO·CH:CH·CO·Me [6]	2260 ‖	14,500	—	—	—

* In $CHCl_3$. † Inflexion. ‡ Minimum. § In *cyclo*hexane. ‖ In hexane.

[1] B. p. 79°/757 mm., $n_D^{20°}$ 1·4071. [2] Scheibe, *Ber.*, 1925, **58**, 586. [3] Braude and Jones, *J.*, 1945, 498.
[4] Dimroth, *Angew. Chem.*, 1939, **52**, 545. [5] Undistilled semi-hydrogenation product of phenyl ethynyl ketone.
[6] M. p. 78°.

Experimental.

Oct-3-yn-2-one (V).—(a) An authentic specimen of oct-3-yn-2-one was prepared by the method of Kroeger and Nieuwland (*J. Amer. Chem. Soc.*, 1936, **58**, 1861); it had the following physical properties: b. p. 74°/12 mm., $n_D^{16°}$ 1·4487 (*idem*, *loc. cit.*, give b. p. 76—76·5°/15 mm., $n_D^{20°}$ 1·4446). The 2 : 4-*dinitrophenylhydrazone* formed orange needles, m. p. 87—88°, from aqueous alcohol (Found: N, 18·4. $C_{14}H_{16}O_4N_4$ requires N, 18·4%). The *semicarbazone* crystallised from aqueous alcohol in needles, m. p. 109° (Found: N, 23·25. $C_9H_{15}ON_3$ requires N, 23·2%). Light absorption in alcohol: Maximum, 2600 A.; ε = 18,500. The *phenylsemicarbazone* formed needles, m. p. 104—104·5°, from aqueous alcohol (Found: N, 16·55. $C_{15}H_{19}O_2N$ requires N, 16·35%). Light absorption in alcohol: Maxima, 2290, 2730 and 2800 A.; ε = 17,000, 29,000 and 28,500, respectively.

(b) A solution of chromium trioxide (10·3 g.) in water (30 c.c.) and concentrated sulphuric acid (8·7 c.c.) was added during two hours to a stirred solution of oct-3-yn-2-ol (15 g.; for preparation, see below) in acetone (30 c.c.) at 5—10°. After stirring for a further 30 minutes, the mixture was diluted with water to 250 c.c. and the product isolated with ether; distillation then gave oct-3-yn-2-one (11·5 g.), b. p. 70·5—71·5°/14 mm., $n_D^{16°}$ 1·4482. The semicarbazone had m. p. 109°, undepressed on admixture with an authentic specimen. The light absorption data of the ketone were identical with those of the material prepared as described above, (a).

Phenyl Ethynyl Ketone (VI; R = Ph).—To a stirred solution of phenylethynylcarbinol (342 g.; Jones and McCombie, *J.*, 1942, 733) in acetone (500 c.c.) a solution of chromium trioxide (175 g.) in water (500 c.c.) and concentrated sulphuric acid (148 c.c.) was slowly added; the operation, carried out at 5° in nitrogen, lasted 3—4 hours. After stirring for a further 30 minutes, the mixture was diluted with water and the product extracted with ether. Evaporation of the ethereal solution gave a yellow solid which was recrystallised from aqueous methanol to give *phenyl ethynyl ketone* (258 g.), as pale yellow needles, m. p. 50—51°, having an odour similar to that of benzaldehyde (Found: C, 83·1; H, 4·45. C_9H_6O requires C, 83·1; H, 4·65%). The 2 : 4-*dinitrophenylhydrazone* formed orange needles, m. p. 214° (decomp.), from benzene–ligroin (b. p. 80—100°) (Found: N, 18·0. $C_{15}H_{10}O_4N_4$ requires N, 18·05%). With alcoholic semicarbazide acetate, phenyl ethynyl ketone gave the *di-semicarbazone* of *hydroxymethylene-acetophenone* as pale yellow plates, m. p. *ca.* 235°. When this material was sublimed at 200° (bath temp.)/10^{-4} mm., it gave colourless needles, m. p. 115°, immediately solidifying and re-melting at 238—239° (Found: N, 32·5. $C_{11}H_{14}O_2N_6$ requires N, 32·05%).

Propyl Ethynyl Ketone (VI; R = Pr).—A solution of chromium trioxide (57 g.) in water (165 c.c.) and concentrated sulphuric acid (48·3 c.c.) was added over a period of 2½ hours to a stirred and cooled solution of propylethynylcarbinol (75 g.; for preparation, see below) in acetone (240 c.c.), the operation being carried out in nitrogen. After stirring for a further 30 minutes, sufficient water was added to dissolve the precipitated chromium salts and the product was isolated by means of ether. Distillation gave *propyl ethynyl ketone* (53 g.) as a colourless mobile liquid with marked sternutatory and lachrymatory properties. It had b. p. 65—66°/100 mm., $n_D^{17°}$ 1·4260 (Found: C, 75·05; H, 8·3. C_6H_8O requires C, 75·0; H, 8·4%). The 2 : 4-*dinitrophenylhydrazone* formed orange needles, m. p. 136—137° from alcohol (Found: N, 20·35. $C_{12}H_{12}O_4N_4$ requires N, 20·3%).

Methyl Ethynyl Ketone (VI; R = Me).—A solution of chromium trioxide (146 g.) in water (380 c.c.) and concentrated sulphuric acid (122 c.c.) was added over a period of 7—8 hours to a stirred solution of methylethynylcarbinol (150 g.; Macullum, U.S.P., 2,125,384) in water (325 c.c.) at 20° in an atmosphere of nitrogen. The mixture was stirred for a further 2—3 hours, set aside overnight and then extracted with ether. The ethereal solution was washed with water, dried and evaporated carefully through a Fenske column and the residue was distilled in nitrogen. The portion boiling below 100° was dried over calcium chloride and fractionation through a Dufton column (24 cm.), employing a partial reflux head, gave methyl ethynyl ketone (55 g.), b. p. 84·5—86°, $n_D^{22°}$ 1·4050 (Petrov, *J. Gen. Chem. Russia*, 1940, **10**, 1682, gives b. p. 83·5—84·5°, $n_D^{20°}$ 1·4070). The *p*-nitrophenylhydrazone formed reddish-brown needles, m. p. 142—143° from aqueous methyl alcohol (*idem*, *loc. cit.*, gives m. p. 140°) (Found: N, 20·85. Calc. for $C_{10}H_9O_2N_3$: N, 20·7%). The 2 : 4-*dinitrophenylhydrazone* formed yellow needles, m. p. 181°, from alcohol (Found: N, 22·65. $C_{10}H_8O_4N_4$ requires N, 22·55%).

Propenyl Ethynyl Ketone (VII).—This was prepared by a procedure analogous to that used for phenyl ethynyl ketone from propenylethynylcarbinol (250 g.; Heilbron, Jones and Weedon, *J.*, 1945, 81) in acetone (500 c.c.), and chromium trioxide (175 g.) and concentrated sulphuric acid (148 c.c.) in water (500 c.c.). Isolation by means of ether gave *propenyl ethynyl ketone* (193 g.) as a pungent smelling, colourless liquid, b. p. 145°/747 mm. and 75—77°/44 mm., $n_D^{20°}$ 1·4770 (Found: C, 76·55; H, 6·75. C_6H_6O requires C, 76·6; H, 6·45%. Determination of active hydrogen (Zerewitinoff): The ketone (99·5 mg.) gave 25·5 c.c. of methane at 21°/766 mm., after heating to 90°, corresponding to 1·0 atom of active hydrogen per mol.). The 2 : 4-*dinitrophenylhydrazone* formed red needles, m. p. 162—163°, from alcohol (Found: C, 52·7; H, 4·1; N, 19·95. $C_{12}H_{10}O_4N_4$ requires C, 52·55; H, 3·7; N, 20·45%).

A solution of the ketone (1 g.) in ethyl acetate (10 c.c.) was shaken with Adams catalyst (10 mg.) and hydrogen until absorption was complete, 744 c.c. of hydrogen being absorbed at 21°/765 mm., corresponding to 2·9 ⊨. Removal of the catalyst and solvent gave ethyl propyl ketone which gave a 2 : 4-dinitrophenylhydrazone, m. p. 133—134°, undepressed on admixture with an authentic specimen.

Hex-3-en-5-yn-2-one (VIII).—A stirred and well cooled solution (0—5°) of hex-3-en-5-yn-2-ol (50 g.; see Part IV) in acetone (100 c.c.) was treated dropwise with a solution of chromium trioxide (35 g.) and concentrated sulphuric acid (29·6 c.c.) in water (100 c.c.) during 2½ hours, in an atmosphere of nitrogen in diffuse light. Isolation in the usual way gave *hex-3-en-5-yn-2-one* (23·5 g.) as a very pale yellow liquid, which rapidly darkened in air and light. It had b. p. 60—63°/20 mm., $n_D^{16°}$ 1·4954 (Found: C, 76·45; H, 6·3. C_6H_6O requires C, 76·6; H, 6·45%. Determination of active hydrogen (Zerewitinoff): the ketone (59 mg.) gave 14·4 c.c. of methane at 22°/765 mm. (*i.e.*, 0·95 atom of active hydrogen per mol.). The 2 : 4-*dinitrophenylhydrazone* formed dark reddish-brown plates, m. p. 181° (decomp.), from alcohol–dioxan (2 : 1) (Found: N, 20·35. $C_{12}H_{10}O_4N_4$ requires N, 20·45%).

A solution of the ketone (2·9 g.) in methyl acetate (20 c.c.) was shaken with Adams catalyst (20 mg.) and hydrogen until absorption (2000 c.c. at 22°/760 mm.) ceased. After filtration and evaporation, the residue gave methyl butyl ketone (1·9 g.), b. p. 128°, $n_D^{18·5°}$ 1·4038. The 2 : 4-dinitrophenylhydrazone crystallised from methyl alcohol in orange needles, m. p. 107—107·5°, undepressed on admixture with an authentic specimen.

5-Methylhex-5-en-3-yn-2-one (IX; R = Me).—(a) A suspension of 2-methylvinylacetylenylmagnesium chloride (from magnesium 7·7 g.) in ether (500 c.c.) was cooled to − 30° and a solution of acetic anhydride (65 g.) in ether (100 c.c.) was gradually added over 2½ hours. The mixture was stirred at − 30° for a further 2 hours and then at − 5° for 2 hours after which ice and water were added and the mixture set aside overnight. The ethereal layer was separated, the aqueous mother liquors were extracted once with ether and the combined ethereal solutions were washed with water and saturated sodium bicarbonate solution until free from acetic acid. The residue on distillation in nitrogen gave two fractions. (i) *5-Methylhex-5-en-3-yn-2-one* (*ca.* 3 g.) was a pungent, colourless mobile liquid, b. p. 73·5°/44 mm., $n_D^{16°}$ 1·4787 (Found: C, 77·65; H, 7·55. C_7H_8O requires C, 77·75; H, 7·45%). The 2 : 4-*dinitrophenylhydrazone* formed orange needles, m. p. 133·5—134·5°, from alcohol (Found: N, 19·2. $C_{13}H_{12}O_4N_4$ requires N, 19·45%). (ii) The *acetate* of 2 : 5 : 8-

trimethylnona-1 : 8-*dien*-3 : 6-*diyn*-5-*ol* (X) (7·5 g.) was a colourless liquid, b. p. 69·5°/0·2 mm., $n_D^{16°}$ 1·5042 (Found : C, 77·5; H, 7·85. $C_{14}H_{16}O_2$ requires C, 77·75; H, 7·45%). Light absorption in alcohol : Maximum, 2230 A.; ε = 22,000.

(b) A suspension of 2-methylvinylacetylenylmagnesium chloride (from magnesium 7·7 g.) in ether (500 c.c.) was slowly added over 2½ hours to a solution of acetic anhydride (65 g.) in ether (150 c.c.), at − 30°. Stirring was continued for 1½ hours at − 30° and then for 2 hours at − 5°. Ice and water were added, the solution was kept overnight and after stirring at room temperature for 4 hours to ensure complete hydrolysis of the excess acetic anhydride, the product was isolated as in (a). Distillation in nitrogen gave 5-methylhex-5-en-3-yn-2-one (8·4 g.), b. p. 73—74°/40 mm. and 42—44°/11 mm., $n_D^{16°}$ 1·4794.

(c) A solution of 5-methylhex-5-en-3-yn-2-ol (10 g.; Nazarov and Elizarova, *Bull. Acad. Sci. U.R.S.S.*, 1940, 189) in acetone (20 c.c.) was cooled to 5° and treated in nitrogen in the usual way with chromium trioxide (6·35 g.) in sulphuric acid (5·3 c.c.) and water (20 c.c.). Isolation by means of ether and distillation gave 5-methylhex-5-en-3-yn-2-one (1·0 g.), b. p. 74°/40 mm., $n_D^{15°}$ 1·4798. The 2 : 4-dinitrophenylhydrazone had m. p. 133·5—134·5°, undepressed on admixture with a specimen from (a).

Hex-5-en-3-yn-2-one (IX; R = H).—A suspension of vinylacetylenylmagnesium chloride (from magnesium 8 g.) in ether (500 c.c.) was added to acetic anhydride (68 g.) in ether (200 c.c.) as described in the case of the methyl analogue (b). *Hex-5-en-3-yn-2-one* was obtained as a colourless, mobile, sternutatory liquid (5·1 g.) that rapidly developed a yellow colouration on standing. It had b. p. 62—63·5°/40 mm., $n_D^{15°}$ 1·4891 (Found : C, 76·35, 76·25; H, 6·65, 6·75. C_6H_6O requires C, 76·6; H, 6·45%). The 2 : 4-*dinitrophenylhydrazone* separated from methanol in orange needles, m. p. 162° (Found : C, 53·0; H, 3·8. $C_{12}H_{10}O_4N_4$ requires C, 52·55; H, 3·7%).

Deca-2 : 8-*dien*-5-*yn*-4 : 7-*dione* (XI).—Deca-2 : 8-dien-5-yn-4 : 7-diol (3 g.; Heilbron, Jones, and Raphael, *J.*, 1943, 268) was oxidised in the usual manner in acetone (20 c.c.) with a solution of chromium trioxide (2·45 g.) in water (10 c.c.) and concentrated sulphuric acid (2·3 c.c.). Isolation by means of ether gave *deca*-2 : 8-*dien*-5-*yn*-4 : 7-*dione* (1·2 g.) as an oil, b. p. 80—81°/0·005 mm., 50° (bath temp.)/10^{-4} mm., $n_D^{21·5°}$ 1·5289 (Found : C, 74·05; H, 6·3. $C_{10}H_{10}O_2$ requires C, 74·05; H, 6·2%. Determination of active hydrogen (Zerewitinoff) : The diketone (49 mg.) gave only 0·5 c.c. methane at 24° and 755 mm. Semimicro-hydrogenation : A solution of the diketone (0·8 g.) in ethyl acetate (10 c.c.) shaken with Adams catalyst (25 mg.) absorbed 476 c.c. of hydrogen at 19°/761 mm. Calc. for 4 |= per mol. : 472 c.c.).

Dec-5-yn-4-ol-7-one (XII).—To a stirred and cooled solution of dec-5-yn-4 : 7-diol (15 g.; for preparation, see below) in acetone (75 c.c.) a solution of chromium trioxide (8·8 g.) in water (45 c.c.) and concentrated sulphuric acid (8·0 c.c.) was added during 2 hours. After stirring for a further 30 minutes the product was isolated by means of ether giving, on distillation, *dec-5-yn-4-ol-7-one* (8·8 g.) as a colourless liquid, b. p. 91—92°/0·4 mm., $n_D^{16°}$ 1·4672 (Found : C, 71·3; H, 9·55. $C_{10}H_{16}O_2$ requires C, 71·4; H, 9·6%). Determination of active hydrogen (Zerewitinoff) : The product (59 mg.) gave 8 c.c. of methane at 21° and 761 mm., *i.e.*, 0·95 atom of active hydrogen per mol.). The 2 : 4-*dinitrophenylhydrazone* crystallised from aqueous methanol in yellow needles, m. p. 84—85° (Found : N, 15·7. $C_{16}H_{20}O_5N_4$ requires N, 16·1%).

Dec-5-yn-4 : 7-*dione* (XIII).—Chromium trioxide (3·0 g.), in water (15 c.c.) and concentrated sulphuric acid (2·7 c.c.) was added over 1½ hours to a stirred solution of dec-5-yn-4-ol-7-one (5·9 g.) in acetone (25 c.c.). Stirring was continued for a further 15 minutes and, after diluting with water, the product was isolated by means of ether. Distillation in nitrogen gave *dec*-5-*yn*-4 : 7-*dione* (1·45 g.), as a pale yellow liquid which polymerised extensively on distillation. It had b. p. 74—75°/0·4 mm., 61·5°/0·3 mm., $n_D^{12·5°}$ 1·4593 (Found : C, 72·25; H, 8·7. $C_{10}H_{14}O_2$ requires C, 72·25; H, 8·5%). With 2 : 4-dinitrophenylhydrazine sulphate, the diketone gave a *derivative* which crystallised from ethyl acetate in orange needles, m. p. 183—184° (Found : N, 20·3. $C_{22}H_{24}O_8N_8$ requires N, 20·55%). Light absorption in chloroform : Maximum, 3870 A.; ε = 45,000.

Decane-4 : 7-*dione*.—(a) A solution of dec-5-yn-4 : 7-dione (325 mg.) in ethyl acetate (10 c.c.) was shaken in hydrogen in the presence of Adams catalyst (10 mg.) until absorption was complete (95 c.c. at 15·5°/780 mm.; theoretical 90 c.c.). After removal of catalyst and evaporation of solvent, the residue was distilled and gave decane-4 : 7-dione (170 mg.), b. p. 53·5°/0·1 mm. The dioxime was crystallised from benzene and had m. p. 108°, undepressed on admixture with the specimen prepared according to (b).

(b) (With G. H. Hargreaves.) Oxidation of decane-4 : 7-diol (4 g.) (obtained by complete hydrogenation of dec-5-yn-4 : 7-diol) with chromic acid in sulphuric acid gave the *diketone* (2·5 g.) which, after distillation at 10^{-4} mm., solidified and had m. p. 22° (Found : C, 70·65; H, 10·6. $C_{10}H_{18}O_2$ requires C, 70·55; H, 10·65%). The *dioxime* was obtained from benzene in flat needles, m. p. 108° (Found : N, 13·9. $C_{10}H_{20}O_2N_2$ requires N, 14·0%). It is appreciably soluble in water.

2-*Methyloct*-6-*en*-3-*yn*-2-*ol*-5-*one* (XV).—A solution of 2-methyloct-6-en-3-yn-2 : 5-diol (10 g.; for preparation, see below) in acetone (40 c.c.) at about 4° was treated during 30 minutes with a solution of chromium trioxide (4·5 g.) in water (22 c.c.) and concentrated sulphuric acid (4 c.c.), stirring was continued for a further 15 minutes and the mixture was diluted with water and the product isolated by means of ether. Distillation gave 2-*methyloct*-6-*en*-3-*yn*-2-*ol*-5-*one* (6·2 g.) as a colourless liquid, b. p. 96—99°/0·03 mm. and 65—66°/0·003 mm., $n_D^{17°}$ 1·4988 (Found : C, 70·4; H, 7·9. $C_9H_{12}O_2$ requires C, 71·05; H, 7·95%). The 2 : 4-*dinitrophenylhydrazone* formed red prismatic needles, m. p. 172—173° from alcohol (Found : C, 54·3; H, 4·85. $C_{15}H_{16}O_5N_4$ requires C, 54·2; H, 4·85%).

1 : 1-*Diphenylhept*-5-*en*-2-*yn*-1-*ol*-4-*one* (XVI).—A stirred solution of 1 : 1-diphenylhept-5-en-2-yn-1 : 4-diol (4 g.; Cymerman, Heilbron, Johnson, and Jones, *J.*, 1944, 141) in acetone (40 c.c.) was treated at *ca.* 0° with chromium trioxide (1 g.) in water (5 c.c.) and concentrated sulphuric acid (0·8 c.c.) during 40 minutes. After stirring for a further 10 minutes and isolation of the product with ether in the usual way a solid (3·85 g.), m. p. 118°, was obtained; this, after fractional crystallisation from aqueous alcohol, yielded 1 : 1-*diphenylhept*-5-*en*-2-*yn*-1-*ol*-4-*one* (2 g.) as colourless needles, m. p. 134°, depressed on admixture with the starting material (Found : C, 82·45; H, 5·9. $C_{19}H_{16}O_2$ requires C, 82·6; H, 5·85%).

Dibenzoylacetylene.—A solution in acetone (15 c.c.) of a mixture (m. p. 129—130°) of the stereoisomers of 1 : 4-diphenylbut-2-yn-1 : 4-diol (2 g.; Dupont, *Ann. Chim.*, 1913, **30**, 507) was cooled to 0—5° and treated over a period of 15 minutes with a solution of chromium trioxide (1·5 g.) in concentrated sulphuric acid (1·36 c.c.) and water (4 c.c.). After shaking for a further 5 minutes, the mixture was diluted to 100 c.c. with water and the pale yellow solid separated and washed well with water to remove all traces of chromium salts. Recrystallisation from either ligroin (b. p. 80—100°) or alcohol gave dibenzoylacetylene (1·8 g.) as very pale yellow leaflets, m. p. 111—112° (Dupont, *Bull. Soc. chim.*, 1914, **15**, 606, gives m. p. 112°).

Propyl Vinyl Ketone.—Propyl ethynyl ketone (30 g.) in methyl acetate (90 c.c.) was shaken in hydrogen in the presence of a palladium on barium sulphate catalyst (4·5 g., 0·3% Pd) until 7·5 litres had been absorbed. After filtration and rapid removal of solvent, the residue was distilled through a Dufton column to give propyl vinyl ketone (21 g.), b. p. 65·5—66°/100 mm., $n_D^{22°}$ 1·4231 (Courtot and Pierron, *Compt. rend.*, 1929, **188**, 1503, give b. p. 88—90°/150 mm., $n_D^{14°}$ 1·4275).

1-*Diethylaminohexan*-3-*one* (cf. Delaby, *Compt. rend.*, 1926, **182**, 140).—Diethylamine (2·25 g.) was slowly added to a solution of propyl vinyl ketone (3 g.) in ether (10 c.c.) and, after 2 days at room temperature, 1-diethylaminohexan-3-one

(3·8 g.), b. p. 101°/18 mm., $n_D^{18\cdot5°}$ 1·4363, was obtained. The picrate crystallised in yellow prisms, m. p. 81—81·5°, from methanol (Delaby, *loc. cit.*, gives m. p. 81°).

1-*Anilinohexan*-3-*one*.—Propyl vinyl ketone (1 g.) and aniline (0·95 g.) were mixed together in ligroin (2 c.c., b. p. 40—60°) and allowed to stand at room temperature for 2 days. The large colourless plates deposited were separated and recrystallised from the same solvent to give 1-anilinohexan-3-one (1·7 g.), m. p. 60—61°, undepressed on admixture with an authentic specimen prepared according to Blaise and Maire (*Bull. Soc. chim.*, 1908, **3**, 660) who give m. p. 60°.

Vinyl Propenyl Ketone.—Propenyl ethynyl ketone (9·4 g.) in ethyl acetate (40 c.c.) was shaken in hydrogen in the presence of a palladium-barium sulphate catalyst (0·94 g., 0·3% Pd) with exclusion of bright light. When the theoretical amount of hydrogen had been absorbed, the catalyst was separated and the solvent removed under reduced pressure at room temperature. Distillation of the residue gave vinyl propenyl ketone (3·5 g.), b. p. 38·5—39·5°/10 mm., $n_D^{18\cdot5°}$ 1·4696 (Nazarov and Okolskaya, *Bull. Acad. Sci. U.R.S.S.*, 1941, 314, give b. p. 30—31°/7·5 mm., $n_D^{20°}$ 1·4690).

Oct-3-*yn*-2-*ol*.—A solution of 1-hexyne (90 g.) in ether (100 c.c.) was added to ethylmagnesium bromide (from 24·3 g. magnesium) in ether (250 c.c.) and the mixture was heated under reflux for 3 hours in nitrogen and then cooled while freshly distilled acetaldehyde (48 g.) in ether (75 c.c.) was added over 30 minutes. After stirring for 2 hours, the solution was set aside overnight. The complex was decomposed with a cold solution of ammonium chloride and isolation of the product with ether gave oct-3-yn-2-ol (104 g.), b. p. 101·5—103°/40 mm., $n_D^{17\cdot5°}$ 1·4503 (Campbell, Campbell, and Eby, *J. Amer. Chem. Soc.*, 1938, **60**, 2882, give b. p. 88°/40 mm., $n_D^{20°}$ 1·4347) (Found: C, 76·15; H, 11·1. Calc. for $C_8H_{14}O$: C, 76·15; H, 11·2%). The *α-naphthylurethane* crystallised from ligroin (b. p. 40—60°) as needles, m. p. 63·5—64·5° (Found: N, 4·5. $C_{19}H_{21}O_2N$ requires N, 4·75%).

n-*Propylethynylcarbinol*.—A solution of sodium (69 g.) in liquid ammonia (1500 c.c.) was converted to sodamide, in the presence of hydrated ferric nitrate (0·6 g.) and sodium oxide (from 2 g. sodium), and then into sodium acetylide in the manner already described (Heilbron, Jones, and Weedon, *J.*, 1945, 81). A solution of butaldehyde (216 g.) in ether (400 c.c.) was then added over 2—3 hours and after stirring for a further 2 hours, the reaction was terminated by the gradual addition of ammonium chloride (165 g.). When the ammonia had evaporated, sufficient water was added to dissolve the inorganic salts and the product was isolated by means of ether. Distillation through a 12 inch Fenske column gave *n*-propylethynylcarbinol (136 g.), b. p. 89°/100 mm., $n_D^{16\cdot5°}$ 1·4382 (Lespieau, *Ann. Chim.*, 1912, **27**, 137, gives b. p. 141°). The *acetyl derivative* (39 g.), prepared from the carbinol (41 g.) and acetic anhydride (43 g.) in pyridine (40 g.), had b. p. 74°/30 mm., and 65·5—66°/19 mm., $n_D^{19°}$ 1·4257 (Found: C, 68·7; H, 8·8. $C_8H_{12}O_2$ requires C, 68·55; H, 8·65%).

Dec-5-*yn*-4 : 7-*diol*.—A slow stream of pure dry acetylene was passed during 24 hours into a stirred ethereal solution of ethylmagnesium bromide (from magnesium 24 g.). A solution of *n*-butaldehyde (72 g.) in ether was then added over a period of 2 hours, stirring was continued for a further 2 hours and the complex was decomposed with ammonium nitrate (180 g.) and ice water. Isolation by means of ether and distillation gave dec-5-yn-4 : 7-diol (63 g.) as a pale yellow viscous oil, b. p. 134—137°/3 mm., $n_D^{17°}$ 1·4694 (Marvel and Williams, *J. Amer. Chem. Soc.*, 1939, **61**, 2716, give b. p. 113—114°/1 mm., $n_D^{20°}$ 1·4678).

2-*Methyloct*-6-*en*-3-*yn*-2 : 5-*diol* (with G. H. Hargreaves).—Propenylethynylcarbinol (106 g.) in ether solution was added during one hour to an ice-cooled ethereal solution of ethylmagnesium bromide (from 48 g. of magnesium), and the mixture was refluxed for 2 hours. After ice-cooling, a solution of acetone (58 g.) in ether was added dropwise (45 minutes), the mixture stirred overnight in nitrogen and finally refluxed for one hour. After cooling to 0°, the Grignard complex was decomposed with ammonium chloride and ice and isolated by means of ether to give the *glycol* (90 g.), b. p. 120°/10^{-3} mm., $n_D^{22°}$ 1·4861 (Found: C, 69·9; H, 8·95. $C_9H_{14}O_2$ requires C, 70·1; H, 9·15%. Determination of active hydrogen (Zerewitinoff): The glycol (57 mg.) evolved 16·8 c.c. of methane at 19°/766 mm., equivalent to 1·9 atoms of active hydrogen per mol.). The glycol exhibited no absorption of appreciable intensity in the ultraviolet.

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IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY, LONDON, S.W. 7. [*Received*, 24*th September*, 1945.]

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14. *Researches on Acetylenic Compounds. Part II.* (A) *The Addition of Amines to Ethynyl Ketones.* (B) *Auxochromic Properties and Conjugating Power of the Amino Group.*

By KENNETH BOWDEN, ERNEST A. BRAUDE, E. R. H. JONES, and B. C. L. WEEDON.

(A) The smooth addition reaction which occurs at room temperature between primary or secondary amines and ethynyl ketones, and also the interaction of hydroxymethylene derivatives of ketones with amines, lead to identical β-aminoethylenic ketones, *e.g.*, R·CO·C:CH ⟶ R·CO·CH:CH·NHPh ⟵ R·CO·CH:CH·OH. Evidence for the structure of these adducts, which in some cases exist in two interconvertible forms (probably geometrical isomerides), is obtained from their highly characteristic light absorption properties and also by hydrogenation to the saturated amino-ketones.

With the conjugated acetylenic ethylenic ketones (XI and XII), addition of diethylamine apparently occurs directly to the acetylenic bond and not, as might be expected, at the extremities of the conjugated system. Also, in compounds in which the ethylenic and acetylenic bonds are cross conjugated with a carbonyl group (*e.g.*, CH_3·CH:CH·CO·C:CH), the addition reaction is restricted solely to the acetylenic bond, even with excess of the amine.

(B) Data for the ultra-violet light absorption of the above β-aminoethylenic ketones and, more generally, of compounds containing alkyl- and aryl-amino groups attached to the terminal carbon atom of aliphatic unsaturated systems are reported and discussed. From many examples, it is clear that alkylamino groups linked directly to an ethylenic bond produce a powerful bathochromic effect, of the same magnitude as, or even greater than, that brought about by conjugation with an additional ethylenic linkage. Thus the near ultra-violet absorption due to the >C:C·N< grouping is similar to that of the butadiene system. This conjugating effect of the amino group is paralleled both by previously observed exaltations of molecular refractivity and by certain chemical properties somewhat akin to those of classical conjugated systems.

(A) *The Addition of Amines to Ethynyl Ketones.*

UNTIL recently ethynyl ketones (II) have been inaccessible, but, now that they can conveniently be obtained (Part I, preceding paper) by oxidation of the corresponding carbinols with chromic acid, a systematic study of their reactions has become possible. André (*Ann. Chim.*, 1913, **29**, 569) observed that substituted acetylenic ketones react with both primary and secondary amines, the addition of the amino group occurring in the

$$R{\cdot}CO{\cdot}C{\equiv}CR' \xrightarrow{R_1R_2NH} R{\cdot}CO{\cdot}CH{:}CR'{\cdot}NR_1R_2 \qquad R{\cdot}CO{\cdot}C{\equiv}CH \longrightarrow R{\cdot}CO{\cdot}CH{:}CH{\cdot}NR_1R_2$$
$$\text{(I.)} \qquad \text{(II.)} \qquad \text{(III.)}$$

β-position to the carbonyl group, giving aminoethylenic ketones of the type (I). As was to be expected it has now been found that the ethynyl ketones (II) also add amines in a similar manner, the addition of primary and secondary amines in ethereal or alcoholic solutions being exothermic. The ease with which addition takes place appears to decrease in the order : R = alkyl > propenyl > phenyl. The amino-ethylenic ketones (III) are usually formed in good yields but the crude products often consist of mixtures of geometrical isomerides; in some cases two distinct forms have been isolated, but in others only a poorer yield, probably of one of the isomeric modifications, has been obtained. Although a few examples of this addition reaction sufficed to demonstrate its nature and general character, the highly interesting light absorption properties (referred to later) of the products rendered desirable the preparation of a considerable range of these substances.

Phenyl ethynyl ketone (II; R = Ph) reacts readily with aniline in methanolic solution to give 1-anilino-3-phenylpropen-3-one (III; R = R_1 = Ph; R_2 = H) identical with the material obtained by Claisen and Fischer (*Ber.*, 1887, **20**, 2192) by condensation of the sodio-derivative of hydroxymethyleneacetophenone with aniline hydrochloride. These authors formulated their product as $Ph{\cdot}CO{\cdot}CH_2{\cdot}CH{:}NPh$, but this was rendered highly improbable by the work of von Auwers and Wunderling (*Ber.*, 1934, **67**, 644), and the present method of preparation and more especially the light absorption properties of the product are consistent only with the conjugated structure. The ethylenediamine adduct, $Ph{\cdot}CO{\cdot}CH{:}CH{\cdot}NH{\cdot}CH_2{\cdot}CH_2{\cdot}NH{\cdot}CH{:}CH{\cdot}CO{\cdot}Ph$ (IV), is also identical with that obtained (Benary, *Ber.*, 1930, **63**, 1576) by the hydroxymethylene-derivative method.

The reaction between methyl ethynyl ketone (II; R = Me) and aniline was unexpectedly complicated. When a cold equimolecular mixture of the two compounds in ether is allowed to stand a crystalline deposit is gradually formed. The melting point of this material is variable and values as high as 118° have been observed. On crystallisation, or merely on standing for a short time in a vacuum in the dark, the m. p. falls, a constant value of 103—104° being attained. This material is subsequently referred to as the β-form of

(V.) $Me{\cdot}CO{\cdot}CH{:}CH{\cdot}NHPh$ $\qquad$ $Me{\cdot}CO{\cdot}CH_2{\cdot}CH{:}NPh$ (Va.)

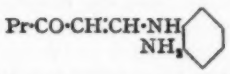
1-*anilinobut*-1-*en*-3-*one* (V) although, in fact, it is probably an equilibrium mixture of constant composition. Evaporation of the ethereal solution, after separation of the β-form, yields a red solid, m. p. *ca.* 85°. Extraction of this material with ligroin, followed by crystallisation from the same solvent or, more conveniently, sublimation of the crude material at 10^{-4} mm., gives the α-form of 1-*anilinobut*-1-*en*-3-*one* (V), m. p. 52—54°. Sublimation of the β-form under similar conditions gives rise to the α-isomer. This α-form is extremely unstable, being gradually converted into the β-form on standing, the melting point rising until the value of 103—104° is attained. The isomerisation is much more rapid in solution or in the molten state. Dissolution of the α-form in cold alcohol or ethyl acetate followed by rapid removal of the solvent under reduced pressure gives a product with m. p. about 90°. The isomerisation is slower in dioxan under identical conditions and from ether, light petroleum, or *cyclo*hexane the α-form is recovered unchanged. On ultraviolet irradiation of an ethereal solution for 2 minutes, however, the solvent being then removed under reduced pressure, appreciable isomerisation takes place, the product having m. p. 84°.

Thielepape (*Ber.*, 1922, **55**, 127) allowed the sodium derivative of hydroxymethyleneacetone to react with aniline hydrochloride and obtained a product, m. p. 91·5°, to which the structure (Va) was assigned. On vacuum distillation, this substance was converted into an isomer, m. p. *ca.* 61°, which, on crystallisation from aqueous alcohol, reverted to the original material (m. p. 91·5°). It seemed probable that Thielepape was dealing with impure α- and β-forms of the 1-anilinobut-1-en-3-one mentioned above, and a repetition of his work showed that this was so. Sublimation (10^{-4} mm.) of the crude product obtained by his method gave the α-form, m. p. 52—54°, which was converted readily into its isomer as already indicated. Kaushal (*J. Indian Chem. Soc.*, 1943, **20**, 53) has also obtained a compound, m. p. 247°, said to have structure (V), by treating ethoxymethyleneacetone with aniline and zinc chloride, but we consider that the material prepared by him cannot have this constitution.

The exact nature of the isomerism of the above α- and β-forms has not yet been established with certainty. The various possibilities include 3- and 5-atom, and also ring chain, prototropy as well as geometrical isomerism. The light absorption properties of the β-form are entirely consistent with the formulation (V) and this is almost certainly true of the α-form, since the same $\lambda_{max.}$ was observed in each case, although variable intensity values were recorded due, doubtless, to the isomerising influence of ultra-violet light. It is well established that geometrical isomers show maximal absorption at practically identical wave-lengths and that marked intensity differences are frequently, though not invariably, observed. The present observations together with the facts concerning the interconversions are reasonably consistent with the postulate of *cis-trans*-isomerism but a complete solution of the problem must await further study.

Addition of β-naphthylamine to methyl ethynyl ketone gives the *adduct* (III; R = Me, R_1 = H, R_2 = β-naphthyl) in good yield and no obvious evidence of the existence of isomeric forms is obtained in this case. The phenomenon is again encountered, however, with the product from the reaction between propyl ethynyl ketone (II; R = Pr[a]) and aniline. The crude material has m. p. 77—78°; on prolonged boiling with ligroin (b. p. 40—60°) it dissolves and, when the solvent is removed, there is left an oil which freezes on cooling, giving crystals which melt below 20°. On keeping a solution of this oil in ligroin at 0° for several days, crystals

(VI.) Pr·CO·CH:CH·NHPh



(VII.)

of 1-*anilinohex*-1-*en*-3-*one*, (VI), m. p. 87—88°, are slowly deposited. If small quantities of the crude material are rapidly dissolved in various hot solvents and the solutions are immediately cooled, the higher melting form crystallises, but prolonged heating appears to effect conversion into the lower melting isomer.

Addition reactions have also been effected between propyl ethynyl ketone and both diethylamine and piperidine, and with *o*-phenylenediamine (equimolecular quantities) the *mono-adduct* (VII) is almost exclusively produced.

Various amine adducts have been prepared from propenyl ethynyl ketone (VIII) using aniline, piperidine, diethylamine and *p*-nitroaniline; with benzidine, a di-adduct was readily obtained. In a number of these examples the yields of pure crystalline adducts were low, presumably due to the presence of stereoisomerides. With this ketone mono-addition could conceivably occur at either the ethylenic or acetylenic linkages; the light absorption of the adducts shows, however, addition at the triple bond as indicated below. This point has been

$$\underset{\text{(VIII.)}}{Me\cdot CH{:}CH\cdot CO\cdot C{\vdots}CH} \xrightarrow{NHR_1R_2} \underset{\text{(IX.)}}{Me\cdot CH{:}CH\cdot CO\cdot CH{:}CH\cdot NR_1R_2} \xrightarrow{H_2/Pt}$$

$$Me\cdot CH_2\cdot CH_2\cdot CO\cdot CH_2\cdot CH_2\cdot NR_1R_2 \xleftarrow{NHR_1R_2} \underset{\text{(X.)}}{Me\cdot CH_2\cdot CH_2\cdot CO\cdot CH_2\cdot CH_2Cl}$$

conclusively proved in the case of the products from the first two amines mentioned above by hydrogenating the adducts (IX) to the saturated amino-ketones (X), which proved to be identical with materials prepared from β-chloroethyl propyl ketone. Further reaction of the adducts (IX) with amines is difficult to effect, the starting materials being recovered unchanged after 24 hours at 100°.

The adducts prepared with diethylamine and piperidine readily form picrates, whereas those obtained from aniline and other aromatic amines do not, and appear to have only weakly basic properties. They are soluble in mineral acids but probably undergo fission and hydration during this process since they cannot be recovered unchanged. With 2 : 4-dinitrophenylhydrazine sulphate, probably owing to its acidic nature, complex products are produced, and even with semicarbazide acetate, in the single case studied (the adduct of propyl ethynyl ketone and piperidine), the product is the bis-semicarbazone of the nitrogen free hydration product.

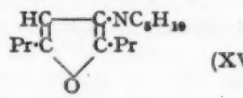
The addition of equimolecular amounts of diethylamine to the three conjugated ethylenic acetylenic ketones (XI and XII; R = H and Me) proceeds smoothly at the ordinary temperature, the addition occurring in each case at the acetylenic linkage. It seemed possible that with (XII; R = H), 1 : 6-addition might lead to the

$$\underset{\text{(XI.)}}{Me\cdot CO\cdot CH{:}CH\cdot C{\vdots}CH} \xrightarrow{NHEt_2} \underset{\text{(XIII.)}}{Me\cdot CO\cdot CH{:}CH\cdot CH{:}CH\cdot NEt_2}; \quad \underset{\text{(XII.)}}{Me\cdot CO\cdot C{\vdots}C\cdot CR{:}CH_2} \xrightarrow{NHEt_2} \underset{\text{(XIV.)}}{Me\cdot CO\cdot CH{:}C(NEt_2)\cdot CR{:}CH_2}$$

same adduct (XIII) as is obtained from hex-3-en-5-yn-2-one (XI), but the two products are different, especially in their light absorption properties (see below).

In the case of the keto-alcohol (XV) addition of piperidine is accompanied by cyclisation (of the hypothetical

$$\underset{\text{(XV.)}}{Pr\cdot CH(OH)\cdot C{\vdots}C\cdot CO\cdot Pr}$$



(XVI.)

intermediate ethylenic keto-alcohol) to the 3-*piperidino*-2 : 5-*dipropylfuran* (XVI), a reaction closely related to certain hydrations described in Part IV of this series (p. 54).

(B) *Auxochromic Properties and Conjugating Power of the Amino Group.*

Light absorption data for the various amino-ethylenic ketones and also for certain αβ-unsaturated amines, all of the general type XCH = CH·NRR′, are given in the accompanying table and figure together with comparative data for the corresponding unsubstituted systems, *i.e.*, XCH = CH_2. The introduction of an amino group at the terminal carbon atom in a conjugated system of the butadiene or methyl vinyl ketone type results in pronounced bathochromic and hyperchromic displacements of maximal absorption (+ Δλ = 500—1000 A; + Δε = 2500—20,000). These are even considerably greater in magnitude than those displacements normally produced —and well exemplified in the literature—by substitution with additional ethylenic or other unsaturated groups. Moreover, even the conjugation of a single ethylenic bond with an amino group, *e.g.*, in (1), results in light absorption equivalent to that exhibited by classical conjugated systems such as butadiene.

The amino group has long been recognised as one of the principal auxochromes in classical colour theory, and its variochromic properties when substituted in aromatic systems are well known. Thus, introduction of an amino group into benzene or pyridine, or into the benzene nuclei of styrene, acetophenone, diphenyl, stilbene, etc., produces displacements of $\lambda_{max.}$ towards higher wavelengths and increases in $\varepsilon_{max.}$ (Pestemer, Langer, and Manchen, *Monatsh.*, 1936, **68**, 326; Pestemer and Mayer-Pitsch, *ibid.*, 1937, **70**, 104; Hertel and Lührmann, *Z. physikal. Chem.*, 1939, **44**, 261); similarly, the successive substitution of amino groups into the benzene nuclei of triphenylmethane dyestuffs results in absorption further and further towards the red region of the visible spectrum. In aliphatic systems, the auxochromic effects of the amino group have hitherto been much less clearly established, although it has recently been shown that the increase in $\lambda_{max.}$ observed in αβ-ethylenic semicarbazones as compared with the parent carbonyl compounds must be ascribed to the conjugating power of the >NH group as such, and not to an extension of the conjugated system through enolisation (Braude and Jones, *J.*, 1945, 498; Burawoy, *J.*, 1941, 20; Evans and Gillam, *J.*, 1943, 565). The substitution in *p*-benzo-

TABLE

Light Absorption of Unsaturated Amines.

(In alcohol except where otherwise stated.)

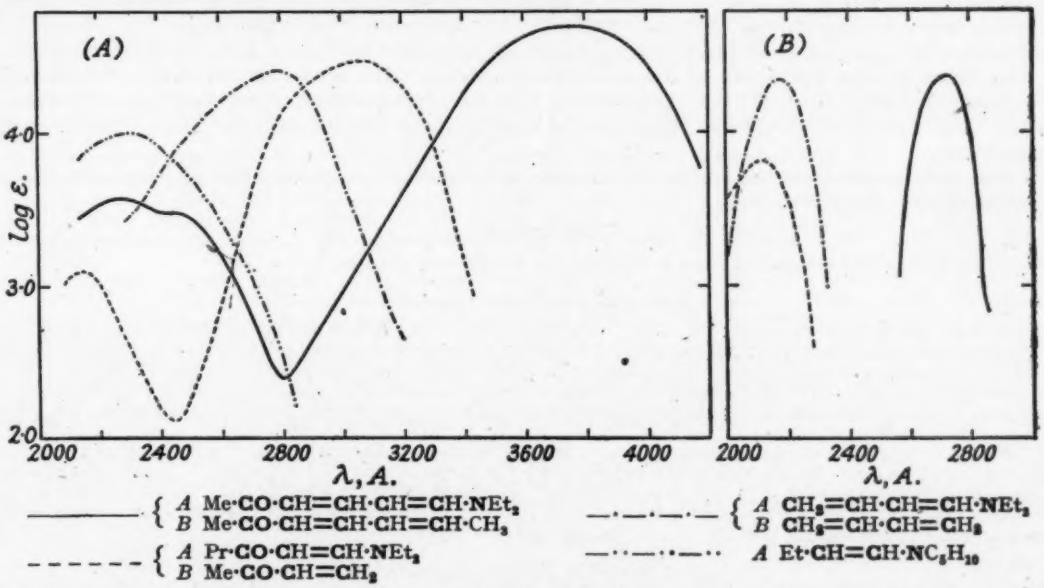
Amine.	$\lambda_{max.}$, A.	$\varepsilon_{max.}$ × 10^{-3}.	Corresponding hydrocarbon or ketone.	$\lambda_{max.}$, A.	$\varepsilon_{max.}$ × 10^{-3}.	$\Delta\lambda$.	$\Delta(\varepsilon \times 10^{-3})$
(1) CHEt=CH·NC_5H_{10} (piperidyl)	2280	100 *	CHEt=CHBu[a1]	1850	80	430	20
(2) CH_2=CH·CH=CH·NEt_2	2810	235 *	CH_2=CH·CH=CH_2 [3]	2170	210	640	25
(3) EtO·C(=O)·CH=CMe·NEt_2	2850 2880	305	EtO·C(=O)·CH=CHMe [3]	2000	200	880	105
(4) Pr·C(=O)·CH=CH·NEt_2	2150 3070	12 280	Me·C(=O)·CH=CH_2 [7]	2100	65	970	215
(5) Pr·C(=O)·CH=CH·NC_5H_{10} (piperidyl)	2300 3080	13 280	,,	2100	65	980	215
(6) Me·C(=O)·CH=CH·NHPh	2280 3380	110 275	,,	2100	65	1280	210
(7) Pr·C(=O)·CH=CH·NHPh	2270 3400	95 245	,,	2100	65	1300	180
(8) Pr·C(=O)·CH=CH·NH·C_6H_4·NH_2 (*o*)	2360 2405 3480	115 115 155	,,	2100	65	1380	90
(9) Me·C(=O)·CH=CH·NH·$C_{10}H_7$ (*β*)	2290 2600 2820 2920 3500	355 115 135 160 315	,,	2100	65	1400	250
(10) CHMe=CH·C(=O)·NEt_2	2150 2420	110 65	MeCH=CH·CH=O [4]	2170	155	−20	−45
(11) Me·C(=O)·CH=CH·CH=CH·NEt_2	2270 2420 3780	35 30 465	Me·C(=O)·CH=CH·CH=CH_2 [5]	2630	220	1150	245
(12) Me·C(=O)·CH=C(NEt$_2$)·CH=CH_2	3080	185	,,	2630	220	450	−35
(13) Me·C(=O)·CH=C(NEt$_2$)·CMe=CH_2	3100 3150	305	Me·C(=O)·CH=CH·CHMe=CH_2	2710	225	440	80
(14) CHMe=CH·C(=O)·CH=CH·NEt_2	2425 3390	105 240	CHMe=CH·C(=O)·CH=CH_2 [7]	2360	95	1030	145
(15) CHMe=CH·C(=O)·CH=CH·NC_5H_{10} (piperidyl)	2420 3420	110 255	,,	2360	95	1060	160
(16) CHMe=CH·C(=O)·CH=CH·NHPh	2400 3770	165 295	,,	2360	95	1410	200
(17) CHMe=CH·C(=O)·CH=CH·NH·C_6H_4·NO_2 (*p*)	2290 2440 3940	120 120 445	,,	2360	95	1580	350
(18) (CHMe=CH·C(=O)·CH=CH·NH·C_6H_4)$_2$	2290 2450 4130	140 140 530	,,	2360	95	1770	435
(19) (Ph·C(=O)·CH=CH·NH·CH_2)$_2$	2420 2450 3450	220 335	Ph·C(=O)·CH=CH_2	2475	105	975	230
(20) Ph·C(=O)·CH=CH·NHPh	2420 2540 3740	175 175 310	,,	2475	105	1265	205

* In hexane.

[1] Platt, Rusoft, and Klevens, *J. Chem. Physics*, 1943, **11**, 535. [2] Smakula, *Angew. Chem.*, 1934, **47**, 657. [3] Grossmann, *Z. physikal. Chem.*, 1924, **109**, 305. [4] Hausser, Kuhn, Smakula, and Hoffer *Z. physikal. Chem.*, 1935, **29**, 371. [5] Calculated from data for Me·CO·(CH:CH)$_2$·**Me** ($\lambda_{max.}$ 2710 A.; ε 22,500; Smakula, *loc. cit.*) assuming effect of methyl group as observed with dienes (Booker, Evans and Gillam, *J.*, 1940, 1453). [6] Assumed to be same as Me·CO·(CH:CH)$_2$·Me. [7] See Part I. (preceding paper).

quinone by amino groups results in a similar displacement of the high intensity absorption band, the latter probably originating in a chromophoric system of the aliphatic type (Braude, *J.*, 1945, 490). Again, in the 2 : 4-dinitrophenylhydrazones of αβ-unsaturated carbonyl compounds, the >NH group permits conjugation between the aliphatic and aromatic portions of the molecule (Braude and Jones, *loc. cit.*).

The present results illustrate in a more direct, simple and conclusive manner that the amino group in aliphatic systems possesses conjugating power similar to that of an ethylenic bond in many respects. This property is clearly to be ascribed to the presence of the unshared electron pair on the nitrogen atom and its capacity to provide a seat for a positive charge. Fixation of this free electron pair by quaternary salt formation completely destroys the powerful auxochromic properties. Thus (1) in 1M-hydrochloric acid solution shows only low intensity absorption above 2100 A. (the original material being recovered from the solution after the measurements (see Experimental)), and this is paralleled by the well known reversion of the ultra-violet absorption of aniline to that of benzene in strongly acid solution. Similarly, neurine bromide, containing a quaternary nitrogen atom adjacent to an ethylenic linkage, shows no high intensity absorption beyond 2100 A. (Castille and Ruppol, *Bull. Soc. Chim. biol.*, 1928, **10**, 639).



Exaltation of molecular refractivity, which is closely related to selective absorption in the ultra-violet, is also observed with αβ-ethylenic amines. The refractivity of β-amino- and β-alkylamino-crotonic esters and of β-amino- and β-alkylamino-αβ-ethylenic ketones has been shown to correspond to the interaction of three conjugated unsaturated groups (Brühl, *Ber.*, 1907, **40**, 878, 1153; Eisenlohr, " Spektrochemie Organischer Verbindungen," Stuttgart, 1912, pp. 111, 153; von Auwers and Susemihl, *Ber.*, 1930, **63**, 1072; Glickmann and Cope, *J. Amer. Chem. Soc.*, 1945, **67**, 1017). The analogy, however, between the spectral properties of the amino group and the ethylenic bond is limited; the conjugating power of the former is not exerted in combination with a second amino group or when attached directly to a carbonyl group. Hydrazine, acetamide and urea exhibit neither high intensity light absorption above 2100 A. nor optical exaltation (Bielecki and Henri, *Compt. rend.*, 1913, **156**, 1860; Braude and Jones, *loc. cit.*; Castille and Ruppol, *loc. cit.*; Brühl, *loc. cit.*; Eisenlohr, *loc. cit.*), and both crotonamide (Bruylants, *Bull. Acad. roy. Belg.*, 1927, **130**, 767) and *N*-diethylcrotonamide (10) have light absorption properties practically identical with those of crotonaldehyde.

The resemblance between the optical properties of $-C=C-C=C-$ and $-C=C-N<$ systems is paralleled by some similarities in chemical properties. Decker and Klauser (*Ber.*, 1904, **37**, 523) and Decker (*ibid.*, 1905, **38**, 2893) suggested and examined the possibility that conjugation existed between ethylenic linkages and the " addition valencies " of adjacent tervalent nitrogen atoms, and Robinson (*J.*, 1916, 1038) provided convincing evidence for this hypothesis by his studies on the *C*-alkylation of certain derivatives of β-aminocrotonic acid, thus :

$$NEt_2\cdot CMe{=}CH\cdot CO_2Et + MeI \longrightarrow I[NEt_2{=}CMe\cdot CHMe\cdot CO_2Et]$$

This terminal addition to the conjugated system is reminiscent of the 1 : 4-addition undergone by diene systems. The strong positive tautomeric (electron repelling) effect of the amino group, exemplified, *inter alia*, by its *ortho-para* directing influence in aromatic substitution, is similarly related to its spectral conjugating power and, like the latter, it is inhibited if the free electron pair is immobilised through quaternary salt formation, *e.g.*, in acid solution.

The data presented in the table may now be considered in somewhat greater detail. Substitution of the piperidyl group into butene and of the diethylamino group into butadiene (1 and 2) results in displacements

of $\lambda_{max.}$ of 430 and 640 A. respectively, $\varepsilon_{max.}$ remaining practically unaltered. In purely ethylenic systems tertiary amino groups thus have a bathochromic effect rather greater than that observed with an ethylenic double bond (*i.e.*, $+ \Delta\lambda = 300$—400 A.) (Euler, Karrer, Klussmann, and Morf, *Helv. Chim. Acta*, 1932, **15**, 502; Hausser, Kuhn, Smakula, and Hoffer, *Z. physikal. Chem.*, 1935, **29**, 371), but no hyperchromic effect is observed. Substitution of tertiary amino groups in the β-position of αβ-unsaturated carbonyl compounds gives rise to larger bathochromic and large hyperchromic shifts ($+ \Delta\lambda = 970$ A.; $+ \Delta\varepsilon = 21{,}500$), and an analogous effect is observed with αβ-unsaturated esters (3) (cf., Glickmann and Cope, *loc. cit.*). Subsidiary bands are also present in all cases. Attachment of dialkylamino groups to the terminal carbon atom of triply conjugated systems (11, 14, 15, 19) results in still larger wavelength displacements ($+ \Delta\lambda = ca.$ 1100 A.) than those observed on substitution in αβ-ethylenic ketones, and the bathochromic effect of the amino group, unlike that of the ethylenic bond (Hausser *et al.*, *loc. cit.*), appears to be enhanced with increasing extent of the conjugated system to which it is attached. As would be expected, however, if the amino group forms a branch of the conjugated system (" cross conjugation ") (12, 13), the bathochromic effect is much smaller ($+ \Delta\lambda = ca.$ 450 A.).

Arylamino groups give rise to larger variochromic effects than alkylamino groups, as well as to subsidiary bands of benzenoid origin (6, 7, 8, 16, 17, 18), and hence the amino group is clearly capable of transmitting conjugation between aliphatic and aromatic systems, as has previously been noted (Braude and Jones, *loc. cit.*). The increments in $\lambda_{max.}$ due to NHPh groups are about 300 A. greater than those due to dialkylamino groups, so that $\Delta\lambda_{Ph}$ is approximately equal to $\Delta\lambda_{C=C}$ in these systems. The benzidine derivative (18) absorbs well into the visible region of the spectrum, the position of the principal maximum corresponding to the interaction of about nine conjugated ethylenic linkages, indicating some transmission of conjugation through the diphenyl group.

The comparative effects of the amino, alkylamino and dialkylamino groups, and of other substituents will be reported in a future publication.

Experimental.

The preparation of the ethynyl ketones is described in the preceding paper.

(i) *Additions to Phenyl Ethynyl Ketone.*

1-*Anilino*-3-*phenylpropen*-3-*one* (III; R = R_1 = Ph, R_2 = H).—A solution of aniline (0·7 g.) in methyl alcohol (15 c.c.) was added gradually to a solution of phenyl ethynyl ketone (1 g.) in methyl alcohol (15 c.c.), the temperature being kept below 45°. The separated solid gave, on crystallisation from methanol, 1-anilino-3-phenylpropen-3-one (1·2 g.) as lemon-yellow needles, m. p. 140—141°, undepressed on admixture with an authentic specimen made by allowing the sodium derivative of hydroxymethyleneacetophenone to react with aniline hydrochloride (Claisen and Fischer, *Ber.*, 1887, **20**, 2192).

N:N′-*Bis*-(2-*benzoylvinyl*)-*ethylenediamine* (IV).—A solution of phenyl ethynyl ketone (3 g.) in methyl alcohol (25 c.c.) was added gradually to ethylenediamine monohydrate (0·8 g.) in methanol (20 c.c.) below 40°. The separated solid when crystallised from methanol gave N:N′-bis-(2-benzoylvinyl)-ethylenediamine (2·5 g.) as pale yellow leaflets, m. p. 142°, undepressed on admixture with a specimen prepared from the sodium derivative of hydroxymethyleneacetophenone and ethylenediamine dihydrochloride (Benary, *Ber.*, 1930, **63**, 1576).

(ii) *Additions to Methyl Ethynyl Ketone.*

1-*Anilinobut*-1-*en*-3-*one* (V).—(a) (cf., Thielepape, *Ber.*, 1922, **55**, 127). A solution of aniline hydrochloride (10·3 g.) in water (75 c.c.) was added to a stirred solution of the sodium derivative of hydroxymethyleneacetone (10 g.) in water (40 c.c.) at 5° in an atmosphere of nitrogen. Isolation of the separated oily product with ether and distillation at 80° (bath temp.)/10^{-4} mm. followed by crystallisation of the resulting solid (4·8 g.) from ligroin (b. p. 40—60°) gave **α-1-*anilinobut*-1-*en*-3-*one*** (4·3 g.), as needles, m. p. 52—54° (Found: C, 74·65; H, 6·7. $C_{10}H_{11}ON$ requires C, 74·5; H, 6·9%).

(b) Aniline (5·5 g.) was slowly added to a cooled solution of the ethynyl ketone (4 g.) in ether (25 c.c.) and after standing for 12 hours at 20° and 2 days at 0° a yellow solid (5 g.), m. p. 108—110°, was obtained (from some experiments crude products with m. p. as high as 118° have been isolated). Recrystallisation from aqueous acetone gave **β-1-*anilinobut*-1-*en*-3-*one*** (4·5 g.) as pale yellow plates, m. p. 103—104·5° (Found: N, 8·85. $C_{10}H_{11}ON$ requires N, 8·7%). Evaporation of the mother liquors gave a red solid (3·4 g.; m. p. *ca.* 85°) from which, on sublimation at 80—90° (bath temp.)/10^{-4} mm. the α-form (1·85 g.), m. p. 52—54°, undepressed on admixture with a specimen obtained by method (a), was obtained.

1-(β-*Naphthylamino*)-*but*-1-*en*-3-*one* (III; R = Me, R_1 = H, R_2 = β-$C_{10}H_7$).—To a solution of β-naphthylamine (21 g.) in ether (350 c.c.) methyl ethynyl ketone (10 g.) was gradually added, and after standing overnight at 20°, evaporation gave a crude product (26 g.), m. p. 104°. Chromatography from a benzene solution on alumina followed by crystallisation from aqueous alcohol gave **1-(β-*naphthylamino*)-*but*-1-*en*-3-*one*** (17 g.) as leaflets, m. p. 140—141° (Found: C, 79·75; H, 6·2. $C_{14}H_{13}ON$ requires C, 79·6; H, 6·2%).

(iii) *Additions to Propyl Ethynyl Ketone.*

1-*Anilinohex*-1-*en*-3-*one* (VI).—The addition of aniline (4·5 g.) to the ketone (4·5 g.) was carried out in alcohol (30 c.c.), the temperature being kept below 40° by ice cooling. After standing overnight at 20° the solvent was removed under reduced pressure and then the residue slowly solidified. A saturated solution in ligroin (b. p. 40—60°) deposited prismatic needles of **1-*anilinohex*-1-*en*-3-*one*** (8 g.), m. p. 87—88°, after standing for several days at 0° (Found: C, 75·7; H, 7·85. $C_{12}H_{15}ON$ requires C, 76·1; H 8·0%).

1-*Diethylaminohex*-1-*en*-3-*one* (III; R = Pr, R_1 = R_2 = Et).—A solution of diethylamine (3·7 g.) in ether (10 c.c.) was added to the ketone (5 g.) in ether (20 c.c.) at 0—10°. After this had stood for some hours at 20°, isolation in the usual manner gave the adduct (8 g.), b. p. 105—106·5°/0·4 mm. (Benary, *Ber.*, 1930, **63**, 1573, gives b. p. 137°/15 mm.), $n_D^{20°}$ 1·5237 (Found: C 70·55; H, 11·15. Calc. for $C_{10}H_{19}ON$: C, 70·9; H, 11·3%).

1-*Piperidinohex*-1-*en*-3-*one* (III; R = Pr, R_1R_2 = C_5H_{10}).—A solution of piperidine (4·5 g.) in alcohol (20 c.c.) was gradually added to the ketone (5 g.) dissolved in alcohol (20 c.c.), the temperature being kept below 20°. Evaporation of the solvent under diminished pressure and distillation of the residue gave **1-*piperidinohex*-1-*en*-3-*one*** (6·8 g.) as a pale

yellow oil, b. p. 145°/1·5 mm., $n_D^{19°}$ 1·5586 (Found : C, 72·95; H, 10·65. $C_{11}H_{19}ON$ requires C, 72·95; H, 10·5%). With semicarbazide acetate in aqueous alcoholic solution the *bis-semicarbazone* of *hexane*-1 : 3-*dione* was obtained as crystals, m. p. 203—204°, from methanol (Found : C, 42·35; H, 6·95; N, 36·7. $C_8H_{16}O_2N_6$ requires C, 42·1; H, 7·05; N, 36·8%).

1-(o-*Aminoanilino*)-*hex*-1-*en*-3-*one* (VII).—The ketone (0·96 g.) and *o*-phenylenediamine (1·08 g.) were mixed in ether (50 c.c.) at 20° and, after the solvent had evaporated, the solid residue was crystallised from ligroin (b. p. 60—80°) giving 1-(o-*aminoanilino*)-*hex*-1-*en*-3-*one* (1·4 g.) as needles, m. p. 81—82°, which gradually decomposed on keeping (Found : C, 70·4; H, 7·85. $C_{12}H_{16}ON_2$ requires C, 70·55; H, 7·9%).

(iv) *Additions to Propenyl Ethynyl Ketone.*

1-*Anilinohexa*-1 : 4-*dien*-3-*one* (IX; R_1 = H, R_2 = Ph).—A solution of aniline (5·75 g.) in alcohol (20 c.c.) was added slowly to the ketone (5·75 g.) in alcohol (50 c.c.) the temperature being kept below 40°. After standing at 20° for 3—4 hours, the solution was diluted with water; resulting oil solidified and on crystallisation from aqueous acetone gave 1-*anilinohexa*-1 : 4-*dien*-3-*one* (8 g.) as small yellow plates, m. p. 117° (Found : C, 77·05; H, 7·0; N, 7·45. $C_{12}H_{13}ON$ requires C, 77·0; H, 7·0; N, 7·5%).

1-*Anilinohexan*-3-*one* (X; R_1 = H, R_2 = Ph).—1-Anilinohexa-1 : 4-dien-3-one (1 g.) in ethyl acetate (50 c.c.) was shaken in hydrogen at atmospheric pressure and temperature with platinic oxide (100 mg.) until absorption ceased (245 c.c. at 17°/755 mm. Calc. 256 c.c.). The catalyst and solvent were removed and the residue crystallised on keeping at 0°; on crystallisation from ligroin (b. p. 40—60°) 1-anilinohexan-3-one (0·7 g.) was obtained as needles, m. p. 59·5—60·5°, undepressed on admixture with an authentic specimen prepared by reaction of β-chloroethyl propyl ketone with aniline (Blaise and Maire, *Bull. Soc. chim.*, 1908, **3**, 660, give m. p. 60°).

1-*Piperidinohexa*-1 : 4-*dien*-3-*one* (IX; R_1R_2 = C_5H_{10}).—Piperidine (4·5 g.) and the ketone (5 g.) were mixed in alcohol (60 c.c.) with cooling. Removal of the solvent under reduced pressure and distillation at 75—80° (bath temp.)/10^{-3} mm. gave a pale yellow oil (4 g.) which solidified on keeping at 0°. On crystallisation from ligroin (b. p. 40—60°), 1-*piperidinohexa*-1 : 4-*dien*-3-*one* (2·1 g.) was obtained as lustrous leaflets, m. p. 56—57° (Found : C, 73·65; H, 9·4; N, 7·55. $C_{11}H_{17}ON$ requires C, 73·7; H, 9·55; N, 7·8%). The *picrate* formed yellow leaflets, m. p. 143—144°, from methanol (Found : C, 50·0; H, 5·0. $C_{17}H_{20}O_8N_4$ requires C, 50·0; H, 4·95%).

1-*Piperidinohexan*-3-*one* (X; R_1R_2 = C_5H_{10}).—(a) On gradually adding piperidine (8·5 g.) to β-chloroethyl propyl ketone (6·7 g., for preparation see below) a vigorous reaction tended to occur and was moderated by cooling to 20°. After adding excess of water, the base was isolated by means of ether and on distillation gave 1-*piperidinohexan*-3-*one* (6·8 g.), b. p. 120°/15 mm., $n_D^{14·5°}$ 1·4692 (Found : C, 72·15; H, 11·5. $C_{11}H_{21}ON$ requires C, 72·1; H, 11·5%). The *picrate* crystallised from alcohol in bright yellow plates, m. p. 94° (Found : C, 49·4; H, 5·85. $C_{17}H_{24}O_8N_4$ requires C, 49·5; H, 5·85%).

(b) A solution of 1-piperidinohexa-1 : 4-dien-3-one (0·5 g.) in ethyl acetate (50 c.c.) was shaken with platinic oxide (50 mg.) in hydrogen until absorption, which was practically theoretical, was complete. After separation of the catalyst and solvent the residue gave a picrate, m. p. 94°, undepressed on admixture with a specimen prepared by method (a).

1-*Diethylaminohexa*-1 : 4-*dien*-3-*one* (IX; R_1 = R_2 = Et).—The reaction between the ketone (9·4 g.) and diethylamine (7·3 g.) was effected in alcohol (50 c.c.) with ice cooling. After 3 hours at 20°, the alcohol was removed under reduced pressure and distillation of the residual oil gave 1-*diethylaminohexa*-1 : 4-*dien*-3-*one* (10·4 g.) as a pale yellow oil, b. p. 144°/1·5 mm., $n_D^{17°}$ 1·5835 (Found : C, 71·8; H, 10·0. $C_{10}H_{17}ON$ requires C, 71·85; H, 10·2%). The *picrate* crystallised from methanol in bright yellow plates, m. p. 134° (Found : C, 48·55; H, 5·25. $C_{16}H_{20}O_8N_4$ requires C, 48·5; H, 5·1%).

1-(p-*Nitroanilino*)-*hexa*-1 : 4-*dien*-3-*one* (IX; R_1 = H, R_2 = *p*-$NO_2{\cdot}C_6H_4$).—A mixture of the ketone (3 g.) and *p*-nitroaniline (4·4 g.) in alcohol (65 c.c.) was kept at room temperature for 6 days and, after precipitation with water and crystallisation from acetone, 1-(p-*nitroanilino*)-*hexa*-1 : 4-*dien*-3-*one* (2 g.) was obtained as bright yellow needles, m. p. 191·5—192·5° (Found : C, 62·2; H, 5·55. $C_{12}H_{12}O_3N_2$ requires C, 62·05; H, 5·2%).

N:N'-*Bis*-(3-*ketohexa*-1 : 4-*dienyl*)*benzidine*.—When a solution of benzidine (5 g.) in alcohol (40 c.c.) was added to the ketone (5 g.) in alcohol (15 c.c.) the temperature of the mixture rapidly rose to 50° and a yellowish solid separated. The reaction was completed by heating to 80° for 10 minutes and, after cooling, the solid was separated, washed with alcohol and crystallised from acetic acid giving N:N'-*bis*-(3-*ketohexa*-1 : 4-*dienyl*)*benzidine* (5·6 g.) as golden plates, m. p. 247—248° (Found : 77·75; H, 6·6. $C_{24}H_{24}O_2N_2$ requires C, 77·45; H, 6·5%). With concentrated hydrochloric acid the solid became deep red, the colour reverting to yellow on addition of water.

Miscellaneous Addition Reactions.

1-*Diethylaminohexa*-1 : 3-*dien*-5-*one* (XIII).—Hex-3-en-5-yn-2-one (3 g.) was added to a solution of diethylamine (2·3 g.) in ether (10 c.c.) and, after 24 hours in the dark at room temperature, the ether was removed and the residue distilled to give 1-*diethylaminohexa*-1 : 3-*dien*-5-*one* (2·6 g.) as a yellow viscous oil, b. p. 109°/0·2 mm. (Found : C, 72·0; H, 10·2. $C_{10}H_{17}ON$ requires C, 71·8; H, 10·25%). The *picrate*, which decomposed in warm solutions, was prepared in cold alcohol and crystallised from cold acetone–ligroin (b. p. 40—60°) in golden plates, m. p. 99—100° (bath preheated to 95°) (Found : C, 48·5; H, 5·05. $C_{16}H_{20}O_8N_4$ requires C, 48·5; H, 5·1%).

3-*Diethylaminohexa*-1 : 3-*dien*-5-*one* (XIV; R = H).—Diethylamine (1·95 g.) was added slowly to hex-5-en-3-yn-2-one (2·5 g.) in ether (20 c.c.) with cooling. After 30 minutes at 0° and 2½ hours at 20°, the solvent was removed and the residue distilled in nitrogen giving 3-diethylaminohexa-1 : 3-dien-5-one (1·75 g.) as a pale yellow oil, b. p. 116—118°/0·6 mm., $n_D^{20°}$ 1·5405, which developed a red colour almost immediately after distillation. It decomposed so rapidly (even at 0° in nitrogen and in the presence of hydroquinone) that analysis was not attempted, neither could a solid picrate be obtained. Nevertheless, the light absorption of a freshly distilled sample (see table) provided adequate proof of its structure.

3-*Diethylamino*-2-*methylhexa*-1 : 3-*dien*-5-*one* (XIV; R = Me).—Diethylamine (2·7 g.) was added very slowly to a cooled solution of 5-methylhex-5-en-3-yn-2-one (4 g.) in ether (25 c.c.). After standing overnight at 20°, evaporation of the ether and distillation of the residue in nitrogen gave 3-*diethylamino*-2-*methylhexa*-1 : 3-*dien*-5-*one* (5 g.) as a pale yellow viscous oil, b. p. 74·5—75°/0·2 mm., $n_D^{19°}$ 1·5363 (Found : C, 72·5; H, 10·45. $C_{11}H_{19}ON$ requires C, 72·9; H, 10·55%). The *picrate* formed large yellow prisms, m. p. 107·5—109° from methyl alcohol (Found : N, 14·0. $C_{17}H_{22}O_8N_4$ requires N, 13·65%).

3-*Piperidino*-2 : 5-*dipropylfuran* (XVI).—The keto-alcohol (2·8 g.) and piperidine (1·4 g.) were mixed in ether (20 c.c.) with cooling (ice) and the mixture was set aside at 20° for 2 days. The product was taken up in ether; the basic material was extracted with N-hydrochloric acid and, after further extraction of the aqueous solution, it was liberated with 2N-sodium hydroxide. This procedure gave 3-*piperidino*-2 : 5-*dipropylfuran* (1·8 g.), b. p. 110°/1 mm., 83°/0·15 mm., $n_D^{17°}$ 1·4909 (Found : C, 76·45; H, 10·45. $C_{16}H_{25}ON$ requires C, 76·5; H, 10·7%). The *hydrochloride*, prepared with dry hydrogen chloride in ethereal solution, sublimed at 70° (bath temp.)/10^{-4} mm. and had m. p. 145·5—146° (decomp.) (Found : N, 5·45. $C_{16}H_{26}ONCl$ requires N, 5·15%).

Intermediates and Spectrographic Reference Compounds.

β-Chloroethyl Propyl Ketone (cf., Kenner and Statham, *Ber.*, 1936, **69**, 16).—*n*-Butyryl chloride (126 g.) was stirred and cooled (ice–salt) and freshly powdered aluminium chloride (158 g.) was added during 30 minutes and stirring and cooling were continued for a further 50 minutes. Dry ethylene was then passed in, the temperature being kept at 20°, until 33 g. had been absorbed after which the mixture was stirred for 30 minutes at 20°. The product was isolated by treatment with ice and extraction with chloroform, and β-chloroethyl propyl ketone (127 g., 80%) was obtained having b. p. 67—68°/11 mm. (Blaise and Maire, *Bull. Soc. chim.*, 1906, **3**, 270, give b. p. 73°/10 mm., 68°/9 mm.).

1-*Piperidino*-1-*butene* (1).—This was prepared according to Mannich and Davidsen (*Ber.*, 1936, **69**, 2106) and had b. p. 84—85°/21 mm., $n_D^{19\cdot5°}$ 1·4860. On dissolution of 1 g. in M-HCl (100 c.c.) the solution showed no absorption with $E^{1\%}_{1\ cm.} > 20$ at 2280 A. After adding a slight excess of M-KOH the original compound (0·6 g.) having b. p. 76—79°/18 mm., $n_D^{22°}$ 1·4845 was recovered.

1-*Diethylaminobutadiene* (2).—The general description of this compound and of its preparation given in the literature (Langebeck *et al.*, *Ber.*, 1942, **75**, 235; cf., Mannich, Handke, and Röth, *Ber.*, 1936, **69**, 2112) does not appear to be satisfactory. It has been found that by treating anhydrous diethylamine with crotonaldehyde at −10° in the presence of anhydrous potassium carbonate the above amine is produced directly in 50% yield, but it polymerises extensively on distillation or on standing at 20°. It has b. p. 74°/20 mm., $n_D^{19°}$ 1·5232. Its structure was confirmed by hydrogenation in *cyclo*hexane with platinic oxide to *N*-diethylbutylamine (b. p. 136—137°), and by the formation of anthraquinone by condensation with α-naphthaquinone, in rather higher yield than that claimed by Langebeck *et al.* (*loc. cit.*).

N-Diethylcrotonamide (10).—Prepared from crotonyl chloride (7 g.) and excess diethylamine in dry ether, the *amide* (8·5 g.) had b. p. 52—55°/0·6 mm., $n_D^{23°}$ 1·4735 (Found: N, 10·3. $C_8H_{15}ON$ requires N, 9·95%).

Ethyl β-Diethylaminocrotonate (3) (cf. Kuckert, *Ber.*, 1885, **18**, 618).—A mixture of ethyl acetoacetate (21 g.) and diethylamine (9 g.) was allowed to stand with anhydrous sodium sulphate during 20 days at 20°. The amino-ester (16 g.) having b. p. 93—95°/0·6 mm., $n_D^{22°}$ 1·5115, was obtained.

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IMPERIAL COLLEGE OF SCIENCE AND TECHONOLOGY, LONDON, S.W. 7. [*Received, September 24th*, 1945.]

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15. *Researches on Acetylenic Compounds. Part III. Diene Additions to Ethynyl Ketones.*

By KENNETH BOWDEN and E. R. H. JONES.

Diels–Alder addition reactions between conjugated dienes and ethynyl ketones take place readily at temperatures over the range 20—120°, excellent yields of the expected αβ-ethylenic ketones (*e.g.*, II, III, and IV) being obtained. Some of the adducts have been dehydrogenated with chloranil in boiling xylene to the corresponding aromatic ketones. With an ethylenic ethynyl ketone selective addition occurs, first at the acetylenic linkage.

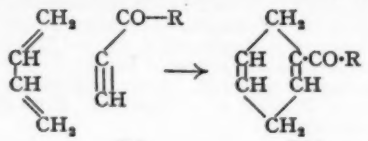
THE employment of acetylenic compounds as dienophiles in the Diels–Alder reaction has been restricted mainly to the use of esters of acetylenedicarboxylic acid (*inter alia*, Diels, Alder, and Nienburg, *Annalen*, 1931, **490**, 236; Lohaus, *ibid.*, 1935, **516**, 295; Alder and Backendorf, *ibid.*, 1938, **535**, 101; Diels and Olsen, *J. prakt. Chem.*, 1940, **156**, 285) and of the acid itself (Brigl and Herrmann, *Ber.*, 1938, **71**, 2280; Diels, Alder, and Nienburg, *loc. cit.*; Alder and Backendorf, *Ber.*, 1938, **71**, 2199). The products obtained with a variety of dienes have been shown to be the expected dihydrophthalic acid derivatives but, in some cases, the primary adducts themselves also function as dienophiles and react with another diene molecule. Propiolic and tetrolic acids have been reacted with *cyclo*pentadiene (Diels and Olsen, *loc. cit.*; Alder *et al.*, *Annalen*, 1936, **525**, 183), but of the acetylenic carbonyl compounds only propiolic and tetrolic aldehydes and dibenzoylacetylene appear to have been used in Diels–Alder reactions. The aldehydes have been condensed with butadienes (F.P. 672,025) giving aldehydo-dihydrobenzenes, while Dupont and Paquot (*Compt. rend.*, 1937, **205**, 805) reacted isoprene and 2 : 3-dimethylbutadiene with dibenzoylacetylene obtaining dibenzoyl-dihydrobenzene derivatives. Comparatively vigorous conditions had to be employed to effect these addition reactions with the acetylenic carbonyl compounds.

During the course of a systematic investigation of the reactions of ethynyl ketones, which are now readily available (see Part I), the Diels–Alder reactions of four of these compounds with various dienes have been examined. Addition takes place fairly readily at temperatures between 20° and 120°, depending mainly upon the particular diene, and the resulting unsaturated cyclic ketones are obtained usually in excellent yields. The ketones are not particularly sensitive to aerial oxidation but, on dehydrogenation with chloranil in boiling xylene (Arnold and Collins, *J. Amer. Chem. Soc.*, 1939, **61**, 1407), the expected benzenoid compounds are produced.

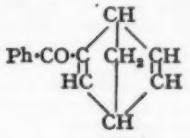
With butadiene at 120°, methyl ethynyl ketone (I; R = Me) gave a 75% yield of 2 : 5-*dihydroacetophenone* (II; R = Me) (2 : 4-*dinitrophenylhydrazone*), and on chloranil dehydrogenation acetophenone was obtained. Under similar conditions, propyl ethynyl ketone (I; R = Pr) gave an almost quantitative yield of 2 : 5-*dihydrobutyrophenone* (II; R = Pr) (2 : 4-*dinitrophenylhydrazone*) which was smoothly dehydrogenated to butyrophenone. In view of the results obtained with the primary adducts from derivatives of acetylenedicarboxylic acid, it was surprising that the dihydroacetophenone was recovered unchanged after heating with an excess of butadiene, even at 170—180° for six hours.

Phenyl ethynyl ketone (I; R = Ph) failed to react with butadiene at 50° (4 hours), but at 120°, 2 : 5-*dihydrobenzophenone* (II; R = Ph) was produced in 75% yield. 3 : 4-*Dimethyl*-2 : 5-*dihydrobenzophenone* was

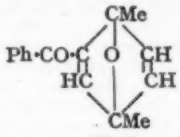
obtained in a similar manner from the ketone and 2 : 3-dimethylbutadiene, and both compounds were dehydrogenated to the expected aromatic ketones with chloranil. With *cyclo*pentadiene an extremely facile addition occurred, 2 : 5-endo*methylene*-2 : 5-*dihydrobenzophenone* (III) being formed at room temperature in practically



(I.) (II.)



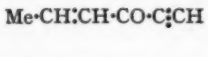
(III.)



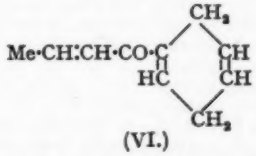
(IV.)

theoretical yield. A corresponding endo-*oxido-compound* (IV), m. p. 89°, was obtained from 2 : 5-dimethylfuran, but more vigorous conditions were necessary in this case. All attempts to react (III) and (IV) with the usual carbonyl group reagents were unsuccessful.

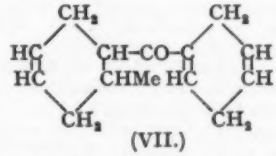
Addition of butadiene to propenyl ethynyl ketone (V) proceeds in two stages, addition apparently occurring first on the acetylenic bond and then subsequently on the ethylenic bond of the propenyl group. When the ketone is treated with an equi-molecular quantity of butadiene at 100°, 1-*crotonyl*-2 : 5-*dihydrobenzene* (VI) (2 : 4-*dinitrophenylhydrazone*) can be isolated in about 20% yield. It does not give a silver compound with ammoniacal silver nitrate and its light absorption properties (see later) also are in accord with the formulation (VI), rather than with the alternative structure arising from addition to the ethylenic linkage in (V). The dual addition reaction takes place with an excess of butadiene at 120—130° leading to 2-*methyl*-1 : 2 : 3 : 6 : 2′ : 5′-*hexahydrobenzophenone* (VII) which on dehydrogenation gives *o*-methylbenzophenone.



(V.)



(VI.)



(VII.)

The light absorption properties (in alcohol solutions) of the αβ-unsaturated ketones mentioned above are indicated in the table. According to the known effects of alkyl substituents (cf. Woodward, *J. Amer. Chem. Soc.*, 1942, **64**, 76; Evans and Gillam, *J.*, 1941, 815) the maximal absorption of ketones of type (II) should be

	$\lambda_{max.}$, A.	$\varepsilon_{max.}$
II; R = Me	2450	5,000
II; R = Pr	2450	3,500
	2500	3,500
VII	2420	3,500
Acetyl*cyclo*hexene	2340	12,000
II; R = Ph	2470	12,500
3 : 4-Dimethyl-2 : 5-dihydrobenzophenone	2290	12,000
	2340 *	11,500
III	2250	6,000
	2500	9,000
	2800	5,500
	2880 *	4,500

	$\lambda_{max.}$, A.	$\varepsilon_{max.}$
IV	*ca.* 2280	*ca.* 8,000
	ca. 2430	*ca.* 8,000
	ca. 2560	*ca.* 9,000
VI	*ca.* 2350	
	ca. 2380	11,000
	ca. 2430	
	ca. 2490	
Me·CH:CH·CO·CH:CH_2	2280	9,500
	2360	9,500

* Inflexion.

located in the region of about 2350 A., as is the case with the closely related acetyl*cyclo*hexene. The marked differences in both location and intensity from the expected values suggest that either the ketones are not αβ-unsaturated (or are impure) or that a hitherto unobserved effect, due to the presence of the second cyclic ethylenic linkage, is operative. The first possibility was carefully examined by converting the ketone (II; R = Pr) into its *semicarbazone*, formed in practically quantitative yield, which showed light absorption (Max. 2600 A., ε = 21,000) typical of the derivative of an αβ-unsaturated ketone (Evans and Gillam, *J.*, 1943, 565). Regeneration from the semicarbazone gave a theoretical yield of the ketone having physical properties identical with those of the starting material. As a consequence, the last explanation is to be preferred and this is rendered the more probable by the known effects of cyclic location on the light absorption properties of conjugated dienes, *i.e.*, maxima at longer wavelengths and markedly reduced intensities.

Experimental.

The preparation of the ketones is described in Part I of this series.

2 : 5-*Dihydroacetophenone* (II; R = Me).—A mixture of methyl ethynyl ketone (6·8 g.) and butadiene (8·1 g.) on being heated in a small autoclave at 120—130° for 3 hours gave, after distillation, 2 : 5-*dihydroacetophenone* (9·15 g.), b. p. 80—81°/14 mm., $n_D^{16°}$ 1·5135 (Found : C, 78·25; H, 8·2. $C_8H_{10}O$ requires C, 78·65; H, 8·25%). The 2 : 4-*dinitrophenylhydrazone* crystallised from benzene in scarlet needles, m. p. 212° (Found : N, 18·4. $C_{14}H_{14}O_4N_4$ requires N, 18·5%). The ketone (2·4 g.) was heated with chloranil (5·4 g.) in boiling xylene (17 c.c.) for 4 hours; the reaction mixture was filtered and, after removal of the solvent under diminished pressure, distillation of the residue gave acetophenone

(1·3 g.), b. p. 77—78°/9 mm., $n_D^{15°}$ 1·5363 (Bruhl, *J. prakt. Chem.*, 1894, **50**, 131, gives b. p. 94·5°/20 mm., $n_D^{19·6°}$ 1·5342). The dinitrophenylhydrazone had m. p. 237°, undepressed on admixture with an authentic specimen.

2 : 5-*Dihydrobutyrophenone* (II; R = Pr).—This was prepared from propyl ethynyl ketone (14·4 g.) and butadiene (8·9 g.), heated together at 120—130° for 3 hours. Distillation gave 2 : 5-*dihydrobutyrophenone* (21·1 g.), b. p. 101—102°/10 mm., $n_D^{18°}$ 1·5010 (Found: C, 79·95; H, 9·4. $C_{10}H_{14}O$ requires C, 79·55; H, 9·3%). The 2 : 4-*dinitrophenylhydrazone* crystallised from dioxan–methanol in scarlet needles, m. p. 176° (Found: N, 16·9. $C_{16}H_{18}O_4N_4$ requires N, 16·95%). The *semicarbazone*, formed in 95% yield by the usual method, crystallised from alcohol in needles, m. p. 173° (Found: N, 20·1. $C_{11}H_{17}ON_3$ requires N, 20·25%). On regeneration, a 95% yield of ketone was obtained having b. p. 119°/20 mm., $n_D^{20°}$ 1·5001 and light absorption properties identical with those of the original material. Dehydrogenation of the ketone (2·0 g.) with chloranil (3·6 g.) as above gave butyrophenone (1·5 g.), b. p. 223° (*lit.* b. p. 220—222°, 218—221·5°). The semicarbazone had m. p. 188—189° (Sorge, *Ber.*, 1902, **35**, 1074, gives m. p. 188°).

2 : 5-*Dihydrobenzophenone* (II; R = Ph).—On heating a mixture of phenyl ethynyl ketone (10 g.) and butadiene (5·2 g.) in an autoclave at 120—130° for 3 hours a semi-solid mass was obtained which was purified by chromatography on a 15 × 1 cm. column of alumina from pentane solution. Evaporation of the eluate and sublimation of the residue at 70° (bath temp.)/10^{-4} mm., gave 2 : 5-*dihydrobenzophenone* (10·5 g.) as a crystalline mass, m. p. 52° (Found: C, 85·05; H, 6·5. $C_{13}H_{12}O_2$ requires C, 84·75; H, 6·55%). The 2 : 4-*dinitrophenylhydrazone*, which formed slowly, crystallised from alcohol–ethyl acetate, in red needles, m. p. 208° (Found: N, 15·0. $C_{19}H_{16}O_4N_4$ requires N, 15·35%). Treated with chloranil (2·7 g.), as above, the ketone (1·8 g.) gave an oil (1 g.) distilling at 70° (bath temp.)/10^{-4} mm., which gave benzophenone 2 : 4-dinitrophenylhydrazone, m. p. 229°, undepressed on admixture with an authentic specimen.

3 : 4-*Dimethyl*-2 : 5-*dihydrobenzophenone*.—Phenyl ethynyl ketone (10 g.) was heated at 120—130° for 3 hours with 2 : 3-dimethylbutadiene (10 g.), giving 3 : 4-*dimethyl*-2 : 5-*dihydrobenzophenone* (11·5 g.) as needles, m. p. 70—71°, from ligroin (b. p. 40—60°) (Found: C, 85·1; H, 7·6. $C_{15}H_{16}O$ requires C, 84·85; H, 7·6%). The 2 : 4-*dinitrophenylhydrazone*, which formed slowly, crystallised from ethyl acetate in small red needles, m. p. 224—225° (Found: N, 14·3. $C_{21}H_{20}O_4N_4$ requires N, 14·3%). Dehydrogenation of the ketone (2·5 g.) with chloranil (2·12 g.) as above gave an oil (2 g.), which distilled at 70°·(bath temp.)/10^{-4} mm., giving the 2 : 4-dinitrophenylhydrazone of 3 : 4-dimethylbenzophenone, m. p. 249° (Allen, *J. Amer. Chem. Soc.*, 1940, **62**, 660, gives m. p. 252°).

2 : 5-endo*Methylene*-2 : 5-*dihydrobenzophenone* (III).—Phenyl ethynyl ketone (6 g.) was mixed with freshly distilled *cyclo*pentadiene (4 g.) at 20°. After a short induction period, reaction ensued and the temperature of the mixture was kept at 20—30° by occasional cooling. On removing the excess of diene under diminished pressure, the residual oil solidified and crystallisation from alcohol or acetic acid gave the *adduct* (9 g.) as leaflets, m. p. 159° (Found: C, 85·45; H, 6·25. $C_{14}H_{12}O$ requires C, 85·7; H, 6·15%).

2 : 5-endo-*Oxido*-2 : 5-*dimethyl*-2 : 5-*dihydrobenzophenone* (IV).—After a mixture of phenyl ethynyl ketone (3·75 g.) and 2 : 5-dimethylfuran (2·9 g.) had been heated in a sealed glass tube at 100° for 3 hours, the product was sublimed at 60° (bath temp.)/10^{-4} mm. and then crystallised from ligroin (b. p. 40—60°) giving the *adduct* (3 g.) as large rectangular plates, m. p. 89° (Found: C, 79·2; H, 6·35. $C_{15}H_{14}O_2$ requires C, 79·6; H, 6·25%).

1-*Crotonyl*-2 : 5-*dihydrobenzene* (VI).—The product, obtained by heating a mixture of propenyl ethynyl ketone (9·4 g.) and butadiene (5·95 g.) at 90—100° for 3 hours, on fractional distillation gave 1-*crotonyl*-2 : 5-*dihydrobenzene* (3 g.), b. p. 112—114°/10 mm., $n_D^{18°}$ 1·5405 (Found: C, 80·6; H, 8·2. $C_{10}H_{12}O$ requires C, 81·0; H, 8·15%). The 2 : 4-*dinitrophenylhydrazone* crystallised from dioxan–methanol in scarlet leaflets, m. p. 191—192° (Found: N, 17·1. $C_{16}H_{16}O_4N_4$ requires N, 17·05%).

2-*Methyl*-1 : 2 : 3 : 6 : 2′ : 5′-*hexahydrobenzophenone* (VII).—After heating propenyl ethynyl ketone (9·4 g.) with butadiene (11·9 g.) at 120—130° for 3 hours the diene polymer was removed by filtration and washed with ether. The filtrate was evaporated and distillation of the residue in the presence of a little hydroquinone gave 2-*methyl*-1 : 2 : 3 : 6 : 2′ : 5′-*hexahydrobenzophenone* (7·2 g.), b. p. 124—125°/1 mm., $n_D^{18°}$ 1·5385 (Found: C, 83·2; H, 8·95. $C_{14}H_{18}O$ requires C, 83·1; H, 8·95%). Heating the ketone (2 g.) with chloranil (8 g.) in the usual way gave, on distillation at 70° (bath temp.)/10^{-4} mm., an oil (0·5 g.) which was converted into its oxime by heating with hydroxylamine hydrochloride (0·5 g.) in pyridine (5 c.c.) for 6 hours on the steam-bath. On crystallisation from aqueous methanol *o*-methylbenzophenone *anti*-oxime (0·45 g.) was obtained as leaflets, m. p. 105° (Smith, *Ber.*, 1891, **24**, 4046, gives m. p. 105°).

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Imperial College of Science and Technology, London, S.W. 7. [*Received, September 24th*, 1945.]

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16. *Researches on Acetylenic Compounds. Part IV. The Hydration of Some Acetylenylcarbinols Derived From αβ-Unsaturated Aldehydes.*

By I. M. Heilbron, E. R. H. Jones, Peter Smith, and B. C. L. Weedon.

Certain acetylenylcarbinols (*viz.*, vinylethynylcarbinol and propenylethynylcarbinol (X)) derived from αβ-unsaturated aldehydes give α-diketones on hydration with sulphuric acid and mercuric sulphate. On similar treatment, the anionotropic rearrangement product of propenylethynylcarbinol, *i.e.*, hex-3-en-5-yn-2-ol (XIII), is isomerised into 2 : 5-dimethylfuran, which can either be isolated as such or converted into acetonylacetone by varying the experimental conditions.

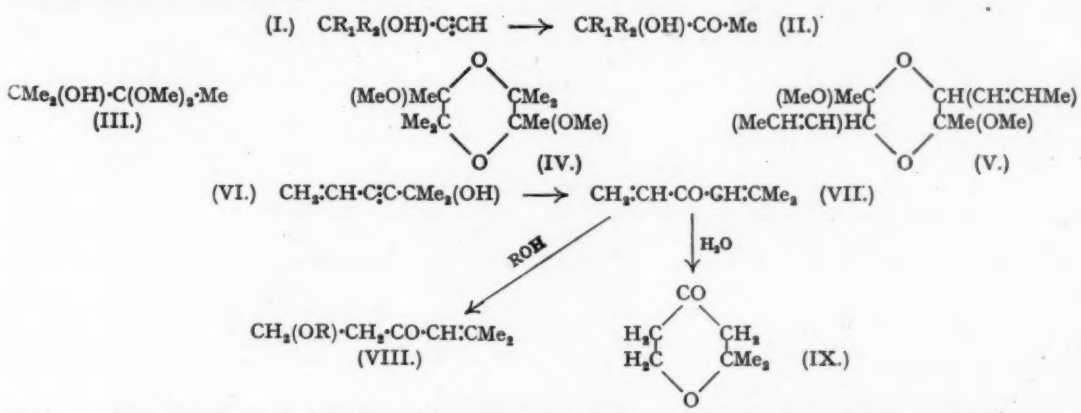
$$CH_2{:}CH{\cdot}CH(OH){\cdot}C{\equiv}CH \longrightarrow Me{\cdot}CH_2{\cdot}CO{\cdot}CO{\cdot}Me$$

$$\text{(XIII.)}\ Me{\cdot}CH(OH){\cdot}CH{:}CH{\cdot}C{\equiv}CH \longrightarrow \text{dimethylfuran} \longrightarrow Me{\cdot}CO{\cdot}CH_2{\cdot}CH_2{\cdot}CO{\cdot}Me$$

The carbinol (XVII) derived from 2-ethylhexenal does not yield an α-diketone, but a furan (XIX) and also a 1 : 4-diketone (XX) are obtained on hydration of either the parent carbinol or its acid-rearrangement product (XVIII). In this case, the highly substituted furan does not appear to undergo hydrolysis to the diketone, and the latter must be formed independently of the furan during hydration. Poor yields of furan are obtained from the substituted carbinol, dec-3-en-5-yn-2-ol (XXII), but the use of the mercuric oxide–boron trifluoride catalyst gives a 30% yield of methylamylfuran.

The hydration of acetylenylcarbinols (I) to α-hydroxyketones (II) has received much attention, the most common method employing dilute sulphuric acid together with mercuric sulphate (Locquin and Sung, *Comp*

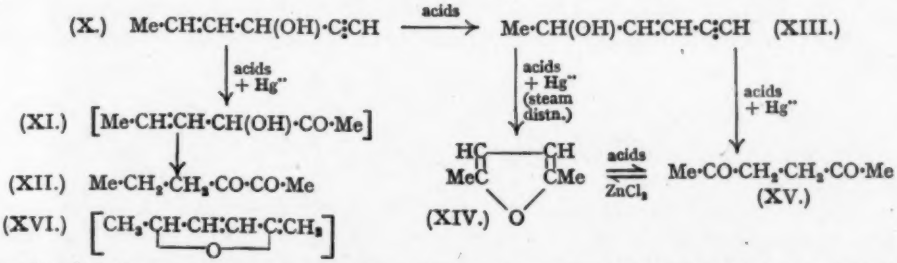
rend., **1923**, **176**, 516; *Rev. gen. sci.*, 1924, **35**, 170; Leers, *Bull. Soc. chim.*, 1926, **39**, 423; Colonge, *ibid.*, 1931, **49**, 441; Rupe and Kambli, *Annalen*, 1927, **459**, 216; Scheibler and Fischer, *Ber.*, 1922, **55**, 2903). Mercuric chloride (Hess and Munderloh, *Ber.*, 1918, **51**, 381) and mercury acetamide (Goldberg and Aeschbacher, *Helv. Chim. Acta*, 1939, **22**, 1185) have been employed for this purpose and mercuric acetate in acetic acid has also been used (Venus-Danilova and Danilov, *J. Gen. Chem. Russia*, 1932, **2**, 645; Ruzicka, Goldberg, and Hunziker, *Helv. Chim. Acta*, 1939, **22**, 707).



Additions of alcohols and carboxylic acids to acetylenic linkages can be effected conveniently by using the mercuric oxide–boron trifluoride catalyst (Hennion, Nieuwland *et al.*, *J. Amer. Chem. Soc.*, 1934, **56**, 1130, 1384, 1786, 1802; 1935, **57**, 2006; 1936, **58**, 80, 892, 1658, etc. For summary, see Spring, *Ann. Reports*, 1942, **39**, 128), and this method has recently been applied to effect the addition of alcohols to simple ethynylcarbinols (Froning and Hennion, *J. Amer. Chem. Soc.*, 1940, **62**, 653; Nazarov and Elizarova, *Bull. Acad. Sci. U.R.S.S.*, 1940, 195). Treatment of dimethylethynylcarbinol (I; $R_1 = R_2 = Me$) with methyl alcohol and the above catalyst gives mainly the hydroxyketal (III) together with some of the substituted dioxan (IV). Hennion and Lieb (*J. Amer. Chem. Soc.*, 1944, **66**, 1289) applied the same process to propenylethynylcarbinol (X), but only the dioxan derivative (V) was isolated, and that in comparatively small yield.

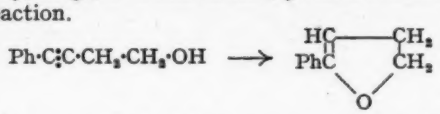
Nazarov and his co-workers (*Bull. Acad. Sci. U.R.S.S.*, 1940, 453, 545, 552; 1941, 314, 423; 1943, 50) have intensively investigated the reactions of vinylacetylenylcarbinols (*e.g.*, VI) in the presence of both mercuric salts and also the mercuric oxide–boron trifluoride catalyst. Under all conditions, the primary reaction involved appears to be isomerisation to the ketone (VII), which may then add alcohols or water to give either alkoxyketones (VIII) or tetrahydropyrone derivatives, such as (IX).

When either propenylethynylcarbinol (X) or vinylethynylcarbinol is treated with mercuric sulphate and dilute sulphuric acid, hydration of the acetylenic bond is apparently accompanied by a simultaneous prototropic rearrangement giving hexane-2 : 3-dione (XII) and pentane-2 : 3-dione (15 and 70% yields, respectively). Under the sole influence of acids, propenylethynylcarbinol has been shown to be isomerised readily to the conjugated vinylacetylenic alcohol (XIII) (Jones and McCombie, *J.*, 1943, 261) but, in the presence of mercuric salts, this isomerisation would, on account of the simultaneous hydration of the acetylenic bond, appear to be suppressed appreciably. The hypothetical intermediate (XI) would not be expected to undergo anionotropic rearrangement readily because of the strongly electron-attracting nature of the carbonyl group. The much slower isomerisation rate of vinylethynylcarbinol accounts for the appreciably higher yield of α-diketone in this case.



The hydration of the rearrangement product (XIII) of propenylethynylcarbinol proceeds in an entirely different manner. When a mixture of hex-3-en-5-yn-2-ol (XIII), mercuric sulphate and dilute sulphuric acid is heated and the product distilled with steam as it is formed, 2 : 5-dimethylfuran (XIV) can be isolated in 45% yield which is raised to 55% by a similar procedure employing aqueous alcoholic mercuric chloride. This process can be regarded either as a direct intramolecular hydration to (XVI) followed by isomerisation to the dimethylfuran, or as comprising normal hydration of the acetylenic linkage, followed by cyclodehydration to [XVI]. The formation of 4 : 5-dihydrofurans as by-products in reactions between acetylenylmagnesium

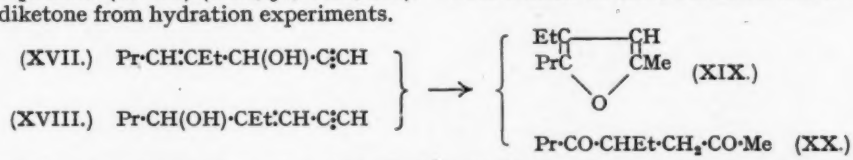
halides and ethylene oxide (Danehy, Vogt, and Nieuwland, *J. Amer. Chem. Soc.*, 1934, **56**, 2790) is in some respects analogous to the above reaction.



Dimethylfuran (25% yield) is also formed when the rearranged carbinol (XIII) is treated with the mercuric oxide–boron trifluoride catalyst in methanol. The poor yield of the dioxan derivative (V) obtained from propenylethynylcarbinol by the same method (Hennion and Lieb, *loc. cit.*) may be attributable to the formation of the furan, the separation of which from the methanol used is not easily effected by distillation, owing to the formation of an azeotrope.

If hex-3-en-5-yn-2-ol (XIII) be heated with mercuric sulphate and sulphuric acid without steam distillation, hydrolysis of the dimethylfuran occurs and acetonylacetone (XV) can be isolated in a yield of about 55%. In the absence of mercuric salts a poor yield of the diketone can be obtained. This conversion can be effected directly from propenylethynylcarbinol (X) by treatment with sulphuric acid followed by the addition of mercuric sulphate, an overall yield of 55% of acetonylacetone being obtained. In the preparation of hexane-2 : 3-dione from propenylethynylcarbinol, some dimethylfuran and appreciable quantities of acetonylacetone are produced simultaneously.

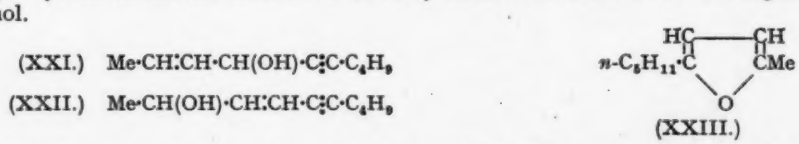
To exemplify further the furan and diketone formation referred to above, a study has been made of the hydration of the ethynylcarbinol (XVII) from 2-ethylhexenal (Jones and McCombie, *J.*, 1942, 733) and its rearrangement product (XVIII) (*idem*, *J.*, 1943, 261). With neither of these carbinols has it been possible to isolate any α-diketone from hydration experiments.



When either the un-rearranged or the rearranged carbinol (XVII or XVIII) is steam-distilled with 1% sulphuric acid, 5-*methyl*-3-*ethyl*-2-n-*propylfuran* (XIX) (*maleic anhydride adduct*) is produced in 20—25% yield, the remainder of the product in each case consisting essentially of the isomerised carbinol (XVIII). No improvement in the yield of furan is obtained by carrying out the steam-distillation under partial reflux or in the presence of mercuric sulphate. Hydration of the unrearranged carbinol (XVII) at 100° with more concentrated acid (10%), in the presence of a comparatively large amount of mercuric sulphate, gives a similar yield of furan, but this is accompanied by 40% of the 1 : 4-diketone, 4-*ethyloctane*-2 : 5-*dione* (XX) (*monosemicarbazone*).

Yields of up to 64% of the furan can be achieved by carrying out the hydration under reflux with 1% acid in aqueous alcohol containing mercuric sulphate, better yields resulting from the use of the rearranged carbinol (XVIII) than from its isomer. As would be expected, refluxing with a solution of mercuric chloride in aqueous alcohol leads to similar results. Some of the diketone (XX) is formed in all of these experiments but the yield never exceeds 25%.

Since hex-3-en-5-yn-2-ol, on hydration, gives 2 : 5-dimethylfuran and acetonylacetone it is clear that, unless the comparatively easily hydrolysable furan is removed from the reaction medium as formed, it is converted into the diketone. This does not apply apparently to the carbinols derived from 2-ethylhexenal. Appreciable yields of the furan are always produced under a wide variety of conditions and all attempts to hydrolyse the furan (XIX) to the diketone (XX) separately have been unsuccessful. The failures are probably related to its very low solubility in aqueous media. The two hydration products would thus appear to be produced by distinct reactions, the diketone formation proceeding most readily in strongly acidic media. There is some evidence that higher yields of the diketone are invariably obtained from the un-rearranged rather than the rearranged carbinol.



Further extension of the hydration experiments to the carbinols (XXI and XXII) derived from condensation of 1-hexyne with crotonaldehyde, followed by rearrangement to give (XXII), resulted in only very poor conversions into the furan. Under most of the conditions mentioned above, the carbinol (XXII) gave, at the most, a 10% yield of 2-*methyl*-5-n-*amylfuran* (XXIII), the bulk of the starting material being recovered unchanged. Prolonged treatment of the rearranged carbinol (XXII) with the mercuric oxide–boron trifluoride catalyst did, however, give a 30% yield of the furan.

Experimental.

Hexane-2 : 3-*dione* (XII).—A mixture of propenylethynylcarbinol (10 g.; Heilbron, Jones, and Weedon, *J.*, 1945, 81), mercuric sulphate (5 g.) and sulphuric acid (100 c.c., 10% w/v) was distilled with steam in an atmosphere of nitrogen.

After saturation of the distillate with salt, isolation by means of ether gave hexane-2 : 3-dione (1·5 g.) as a yellow oil, b. p. 128—130° (Dufraisse and Moureu, *Bull. Soc. chim.*, 1927, **41** 1375, give b. p. 127·5—129°). The dioxime crystallised from aqueous alcohol in needles, m. p. 169—170° (Fileti and Ponzio, *Gazzetta*, 1895, **25**, 242, give m. p. 170—171°) (Found : N, 18·4. Calc. for $C_6H_{12}O_2N_2$: N, 18·4%). The *mono*-2 : 4-*dinitrophenylhydrazone* separated from either aqueous alcohol or ligroin (b. p. 100—120°) as pale yellow needles, m. p. 101—102° (Found : N, 19·5. $C_{12}H_{14}O_5N_4$ requires N, 19·05%). The *quinoxaline derivative* prepared from the diketone and *o*-phenylenediamine in ethereal solution, crystallised from aqueous methanol in buff-coloured prisms, m. p. 63—64° (Found : N, 14·75. $C_{12}H_{14}N_2$ requires N, 15·05%).

Pentane-2 : 3-*dione*.—A mixture of vinylethynylcarbinol (6·3 g.; Jones and McCombie, *J.*, 1942, 733) and mercuric sulphate (1 g.) in sulphuric acid (50 c.c., 10% w/v) was heated on the steam-bath for an hour after which it was distilled until the distillate was colourless. The distillate was saturated with salt giving pentane-2 : 3-dione (5·4 g.), b. p. 110—112°, $n_D^{19°}$ 1·4081 (Dufraisse and Moureu, *loc. cit.*, give b. p. 110—112° and Brühl, *J. pr. Chem.*, 1894, **50**, 140, gives $n_D^{18°}$ 1·40135). The dioxime formed needles, m. p. 172—173° from aqueous alcohol (Fileti and Ponzio, *loc. cit.*, give m. p. 172—173°) and the osazone was obtained from aqueous alcohol as pale yellow prisms, m. p. 165—166° (von Pechmann and Dahl, *Ber.*, 1890, **23**, 2426, give m. p. 166—167°). The *quinoxaline derivative*, prepared in boiling acetic acid, crystallised from aqueous methanol in yellow prismatic needles, m. p. 53—54° (Found : N, 16·45. $C_{11}H_{12}N_2$ requires N, 16·3%). The *bis*-2 : 4-*dinitrophenylhydrazone* separated from aqueous dioxan in small dark red prisms, m. p. 280—281° decomp. (Found : N, 24·6. $C_{17}H_{16}O_8N_8$ requires N, 24·35%).

2 : 5-*Dimethylfuran* (XIV).—(*a*) An authentic specimen, prepared in 46% yield from acetonylacetone (7 g.) and anhydrous zinc chloride (3 g.), by the method of Dietrich and Paal (*Ber.*, 1887, **20**, 1085) who obtained a 25% yield, had b. p. 93—94°, $n_D^{19°}$ 1·4424 (von Auwers, *Annalen*, 1915, **408**, 271, gives b. p. 93—94°, $n_D^{21·6°}$ 1·43508; Nasini and Carrara, *Gazzetta*, 1894, **24**, 271, give $n_D^{17·7°}$ 1·4427). In spite of repeated crystallisation from ether and sublimation at 50° (bath temp.)/10^{-4} mm., the maleic anhydride adduct had m. p. 73° (Diels and Alder, *Ber.*, 1929, **62**, 560, give m. p. 78°). Light absorption in alcohol : Max. 2195 A. ; $\varepsilon = 8000$.

(*b*) Steam was passed slowly into a mixture of hex-3-en-5-yn-2-ol (10·4 g. ; see below for improved method of preparation), mercuric sulphate (200 mg.) and sulphuric acid (40 c.c. ; 0·5% w/v) until the distillate (total volume *ca.* 12 c.c.) no longer separated into two layers. The upper layer was removed, dried over calcium chloride and distilled (finally from sodium) giving 2 : 5-dimethylfuran (4·6 g.), b. p. 93·5—94°, $n_D^{19°}$ 1·4420, which had light absorption properties as described above.

(*c*) A solution of hex-3-en-5-yn-2-ol (20 g.) and mercuric chloride (1·5 g.) in water (60 c.c.) and alcohol (55 c.c.) was stirred and heated on the steam-bath in such a manner as to maintain a slow rate of distillation. A further quantity of mercuric chloride (1·5 g.) was added after 2 hours and the distillation continued until the distillate no longer separated into two layers on dilution with water. The distillate was poured into brine and the upper layer separated, washed with water and dried over calcium chloride. Distillation gave 2 : 5-dimethylfuran (11·4 g.), b. p. 94—96°, $n_D^{23°}$ 1·4417.

(*d*) The catalyst, prepared by heating together for a few minutes a mixture of mercuric oxide (2 g.), boron trifluoride–ether complex (0·8 c.c.) and methanol (0·8 c.c.) together with a few crystals of trichloroacetic acid (cf. *e.g.*, Hennion and Lieb, *loc. cit.*), was dissolved in methanol (80 c.c.) and a solution of hex-3-en-5-yn-2-ol (33 g.) in the same solvent (80 c.c.) was added during an hour at 50—55°. Stirring was continued for another hour at this temperature, powdered potassium carbonate (5 g.) was added and after 30 minutes, the solid material was allowed to settle. The decanted solution was carefully fractionated through an 18 inch column packed with glass helices and the fraction having b. p. 61—65° was freed from methanol by washing with water. Drying over calcium chloride followed by distillation from sodium gave 2 : 5-dimethylfuran (9 g.), b. p. 93—94°, $n_D^{17°}$ 1·4432. Some 12 g. of hex-3-en-5-yn-2-ol were recovered.

Acetonylacetone (XV).—(*a*) An authentic specimen prepared from diethyl diacetosuccinate according to Knorr (*Ber.*, 1900, **33**, 1219) had b. p. 190°/780 mm., 75°/13 mm., $n_D^{17·5°}$ 1·4286, constants in reasonable agreement with the published values.

(*b*) A mixture of hex-3-en-5-yn-2-ol (10·7 g.), mercuric sulphate (0·2 g.) and sulphuric acid (40 c.c. ; 2% w/v) was heated on the steam-bath with vigorous stirring in an atmosphere of nitrogen until it became homogeneous (4—5 hours). After saturation with salt the product was isolated with ether giving acetonylacetone (7·2 g.), b. p. 75—76°/14 mm., $n_D^{15°}$ 1·4292. The dioxime had m. p. 138°, undepressed on admixture with an authentic specimen (Lipp and Schiller, *Ber.*, 1909, **42**, 1967, give m. p. 137°).

(*c*) A mixture of propenylethynylcarbinol (10·2 g.) and dilute sulphuric acid (40 c.c., 2% w/v) was heated on the steam bath with vigorous stirring in an atmosphere of nitrogen for 30 minutes. After addition of mercuric sulphate (0·2 g.), heating and stirring were continued for a further 2—3 hours. Isolation as described above gave acetonylacetone (6·7 g.), b. p. 78—79°/16 mm., $n_D^{18°}$ 1·4289. The dioxime had m. p. 138°, undepressed on admixture with an authentic specimen.

Improved Preparation of Hex-3-en-5-yn-2-ol (XIII) (cf. Jones and McCombie, *J.*, 1943, 261).—A mixture of propenylethynylcarbinol (150 g.) and sulphuric acid (400 c.c., 1% w/v) was distilled with steam and the product was isolated by extraction of the distillate with ether after saturation with salt. This procedure yielded hex-3-en-5-yn-2-ol (120 g.), b. p. 79—81°/30 mm., $n_D^{18·5°}$ 1·4842.

5-*Methyl*-3-*ethyl*-2-n-*propylfuran* (XIX).—When either 4-ethyloct-4-en-1-yn-3-ol (XVII) (Jones and McCombie, *J.*, 1942, 733) or 5-ethyloct-5-en-7-yn-4-ol (XVIII) (Jones and McCombie, *J.*, 1943, 261) was steam distilled in the presence of dilute sulphuric acid (1% w/v), in addition to (XVIII), a 20—25% yield of 5-*methyl*-3-*ethyl*-2-n-*propylfuran* was usually obtained. After distillation from sodium this had b. p. 64°/13 mm., $n_D^{18°}$ 1·4562 (Found : C, 79·1 ; H, 10·8. $C_{10}H_{16}O$ requires C, 78·9 ; H, 10·6%). Light absorption in alcohol : Max. 2210 A. ; $\varepsilon = 9000$. The *maleic anhydride adduct* was prepared by mixing equivalent quantities of the two reactants in ether at −10° and allowing to stand for several days at 0°. The solvent was removed under reduced pressure at −10° and the viscous product solidified after several days at 0° (cf. Butz, *J. Amer. Chem. Soc.*, 1935, **57**, 1314). Recrystallisation from a cooled mixture of ether and pentane gave small plates, m. p. 51·5—52·5° (Found : C, 67·1 ; H, 7·2. $C_{14}H_{18}O_4$ requires C, 67·2 ; H, 7·25%).

5-*Methyl*-3-*ethyl*-2-n-*propylfuran and* 4-*Ethyloctane*-2 : 5-*dione* (XX).—(*a*) A mixture of 4-ethyloct-4-en-1-yn-3-ol (10 g.), dilute sulphuric acid (100 c.c., 10% w/v) and mercuric sulphate (1·0 g.) was stirred vigorously on the steam bath for 5 hours. Isolation by means of ether gave the furan (2·9 g.), b. p. 68—70°/16 mm., $n_D^{16°}$ 1·4560, together with somewhat impure 4-ethyloctane-2 : 5-dione (4·7 g.), b. p. 110—112°/16 mm., $n_D^{16°}$ 1·4570. Repeated fractionation of a larger amount of the latter product gave pure 4-*ethyloctane*-2 : 5-*dione* as a very pale yellow oil, b. p. 110°/18 mm., $n_D^{16°}$ 1·4563 (Found : C, 70·3 ; H, 10·75. $C_{10}H_{18}O_2$ requires C, 70·6 ; H, 10·7%). Light absorption in alcohol : Maxima, 2280, 2750 and 2820 A. ; $\varepsilon = 3000$, 320 and 340 respectively. With semicarbazide acetate in aqueous alcoholic solution the diketone formed a *monosemicarbazone*, m. p. 155·5°, after crystallisation from aqueous alcohol (Found : N, 18·3. $C_{11}H_{21}O_2N_3$ requires N, 18·5%). Light absorption in alcohol : Maximum 2280 A. ; $\varepsilon = 18{,}500$.

(*b*) A mixture of 5-ethyloct-5-en-7-yn-4-ol (10 g.), alcohol (45 c.c.), dilute sulphuric acid (30 c.c., 1% w/v) and mercuric sulphate (0·2 g.) was refluxed for 5 hours. In some experiments (possibly due to variations in the order of mixing of the reagents) mercury was rapidly deposited and the addition of a further 0·2 g. of mercuric sulphate was necessary. Dilution with water and ether extraction gave the furan (6·4 g.), b. p. 68—70°/13 mm., $n_D^{16°}$ 1·4571, and the diketone (2·1 g.), b. p. 108—112°/13 mm., $n_D^{16°}$ 1·4570.

4-Ethyloct-4-en-1-yn-3-ol, similarly treated, gave the furan (5·0 g.), b. p. 68—72°/16 mm., $n_D^{18°}$ 1·4565, and the diketone (2·5 g.), b. p. 106—110°/16 mm., $n_D^{18°}$ 1·4590.

(*c*) A mixture of 5-ethyloct-5-en-7-yn-4-ol (10 g.), water (30 c.c.), alcohol (45 c.c.) and mercuric chloride (0·5 g.) was stirred on the steam-bath for 5—6 hours, during which time four portions, each of mercuric chloride (0·2 g.), were added. Dilution and ether extraction gave the furan (6·0 g.), b. p. 67—69°/13 mm., $n_D^{14°}$ 1·4580, and the diketone (1·0 g.), b. p. 103—106°/13 mm., $n_D^{14°}$ 1·4562.

Similarly 4-ethyloct-4-en-1-yn-3-ol gave the furan (4·7 g.), b. p. 68—72°/15 mm., $n_D^{18°}$ 1·4571, and diketone (2·7 g.), b. p. 108—110°/17 mm., $n_D^{18°}$ 1·4560.

2-Methyl-5-n-amylfuran (XXIII).—(*a*) When subjected to any of the treatmeuts described above, dec-3-en-5-yn-2-ol (XXII) (Heilbron, Jones, and Raphael, *loc. cit.*) gave yields of the furan of the order of 10%, the carbinol being largely recovered unchanged. The pure *2-methyl-5-n-amylfuran*, on distillation from sodium, had b. p. 88°/30 mm., $n_D^{17°}$ 1·4548 (Found: C, 79·0; H, 10·75. $C_{10}H_{16}O$ requires C, 78·9; H, 10·6%). Light absorption in alcohol: Maximum, 2200 A.; $\varepsilon = 8500$. The maleic anhydride adduct dissociated too readily for it to be isolated in the pure state.

(*b*) Dec-3-en-5-yn-2-ol (30 g.) in methanol (80 c.c.) was added to the mercuric oxide–boron trifluoride–trichloroacetic acid catalyst (from 1 g. of mercuric oxide) in the usual manner. Stirring at 50—55° was continued for a further 3 hours after addition was complete (during which time two 1 g. portions of mercuric oxide and a further 0·4 c.c. of the boron trifluoride–ether complex were added) and finally at 20° for 15 hours. After pouring into water and extracting with ether, the residue was steam-distilled to separate the desired product from tarry material. Extraction of the distillate with ether yielded 2-methyl-5-*n*-amylfuran (10 g.), b. p. 64—68°/10 mm., $n_D^{18°}$ 1·4548, together with unchanged starting material (7·5 g.).

The authors thank the Rockefeller Foundation and I.C.I. Ltd., Dyestuffs Division, for financial assistance. They also thank Dr. J. T. McCombie for assistance in the early stages of the above work. Light absorption data were measured by Dr. E. A. Braude.

IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY, LONDON, S.W. 7. [*Received, September 27th*, 1945.]

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17. *Experiments in the Piperidine Series. Part III.*

By R. M. ANKER and A. H. COOK.

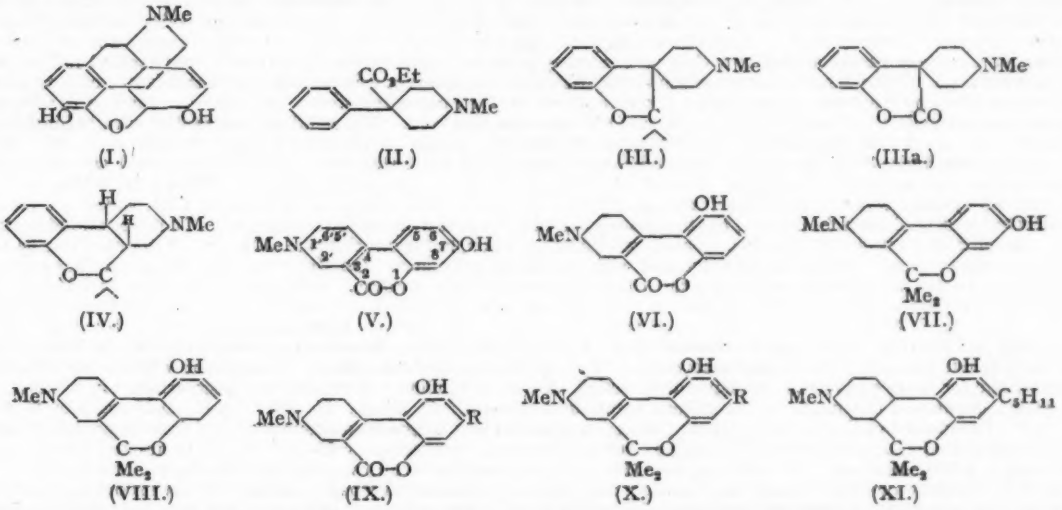
3-Carbethoxy-1-methyl-4-piperidone and the corresponding 3-cyano compound have been condensed with resorcinol to give isomeric 3 : 4-3′ : 4′-tetrahydropyridocoumarins (V, VI) which were converted into *gem*-dimethylpyran derivatives (VII, VIII). 7-Alkyl derivatives of (VI) and (VIII) were obtained by using orcinol or olivetol in place of resorcinol but similar reactions with 4-*n*-hexylresorcinol were unsuccessful. The 7-amyl analogue of (VIII) was reduced to the hexahydropyrido compound which was of special interest as a possible analgesic in view of a skeletal similarity to hexahydrocannabinol and a spatial similarity to morphine.

CONSIDERATION of the structural formulæ of morphine (I) and dolantin (II) suggested that their analgesic action might have been conditioned at least in part by the feature, common to both, of an aromatic grouping in the 4-position of a piperidine ring and maintained in two-dimensional angular relationship to it. In dolantin the relationship may be assumed because of the bulk of the *tert.*-ester group preventing free rotation, and it is possibly significant that active piperidines related to dolantin (Schaumann, *Arch. f. exp. Path. Pharm.*, 1940, **196**, 109) contain, in addition to the 4-aryl group, a large ester or ketone grouping in the 4-position which may have a similar function. In morphine the relationship is necessitated by the additional rings. Similar piperidines which would be constrained to possess a rigid three-dimensional structure can be evolved, the synthesis of which would help to test the correctness of this hypothesis. For example, by discarding atomic groupings in (I) which are probably unessential for analgesic action, the structure (III) can be devised with the postulated angularity; the lactone (IIIa) would be of this type. Consideration was given to this structure and its synthesis during the present work, but as experiments in a rather similar direction have already been reported (Bergel, Haworth, Morrison, and Rinderknecht, *J.*, 1944, 261), their prosecution has been discontinued. It is a short step, however, to the related but still angular structure (IV), and experiments towards this objective are now reported. Additional interest is lent to the ring-structure present in (IV) by the occurrence of a sterically similar system in hexahydrocannabinol, and the synthetic route adopted in the present work was analogous to one which has been extensively used in the cannabinol field.

Ethyl 1-methyl-4-piperidone-3-carboxylate hydrochloride was condensed with resorcinol in presence of concentrated sulphuric acid and phosphorus oxychloride. The pseudo-acidic product was analytically in agreement with the structure (V) and it contained a free hydroxyl group giving a *monomethyl ether*. The orientation (V), rather than the alternative (VI), seemed correct, as the compound failed to give a positive indophenol reaction (Gibbs, *J. Biol. Chem.*, 1927, **72**, 649).

A previous communication (Cook and Reed, *J.*, 1945, 399) described the preparation of 4-imino-3-cyano-1-methylpiperidine and 3-cyano-1-methyl-4-piperidone and, since it was more convenient to obtain these than the ester used above, their reaction with resorcinol was examined. The former piperidone derivative could not be condensed with resorcinol satisfactorily, but the latter gave a *compound* isomeric with (V) above. There could be little doubt that this compound was also a coumarin for the preparation of coumarins from resorcinols and β-ketonitriles is well known (see, for example, Pechmann, *Ber.*, 1883, **16**, 2126; Baker, *J.*, 1927, 2898); moreover a xanthone structure, the only reasonable alternative, was disproved by lactonic properties and the results of reaction with methylmagnesium iodide (see below). Although decomposing at about the same temperature as its isomeride, the new compound showed by contrast with (V) a strongly positive indophenol reaction and was therefore assumed to contain a hydroxyl with a free *p*-position. It yielded a characteristic

methyl ether, distinct from that of (V), but as the light absorption characteristics of the parent condensation products were identical, the same ring system must be postulated for them, and structure (VI) is assigned to the second product.



Compounds (V) and (VI) may assume an angular configuration by migration of the isolated double linking, but they need not necessarily do so and indeed their light absorption indicates, as would be expected on other grounds, that this does not occur. Attempts to impose this angular restriction on the molecule by catalytic reduction with platinum at up to 7 atm. were, however, unsuccessful. Furthermore, experiments to obtain the desired hydro-derivatives or isomerides thereof by condensation of the substituted piperidones with dihydroresorcinol, 5-methyl-, or 5 : 5-dimethyl-dihydroresorcinol, or dihydro-orcinol were fruitless. The methods of reduction were restricted in view of the desirability of *cis* reduction, for *trans* isomerides of type (IV) would be virtually uniplanar. Each of the coumarins was treated with excess of methylmagnesium iodide to obtain the *gem*-dimethyl pyran derivatives (VII), (VIII) analogous to tetrahydrocannabinol. Although some of these and the following compounds were tested for analgesic activity by the courtesy of I.C.I. Ltd. (Dyestuffs Division), there was no notable response, but it still appeared desirable to insert alkyl residues into the aromatic ring as have been found favourable in the cannabinol structures.

In the first place, orcinol condensed smoothly with the piperidone ester hydrochloride; the coumarin gave a positive indophenol reaction and had therefore the anticipated structure (IX) (R = Me). This was also converted into the gem-*dimethylpyran derivative* (X) (R = Me). With these models therefore olivetol (Anker and Cook, *J.*, 1945, 311) was similarly condensed to give the lactone (IX) ($R = C_5H_{11}$) and thence converted into the gem-*dimethylpyran derivative* (X) ($R = C_5H_{11}$), first obtained as its *hydriodide*. Several attempts were made to hydrogenate the isolated double bond in the earlier *gem*-dimethyl compounds, but these were unsuccessful, perhaps because of the low solubility of the compounds. The compound (X) ($R = C_5H_{11}$), however, differed markedly in its physical nature from its predecessors and it was fairly readily hydrogenated. The *dihydro-compound*, characterised as its *acetate*, still showed benzenoid light absorption, and was therefore formulated as (XI), having a necessarily angular structure if it be assumed, as is almost certainly the case, that the use of platinum results in *cis*-reduction.

No homogeneous product was obtained from the condensation of phloroglucinol with the piperidone ester hydrochloride using a mixture of sulphuric acid and phosphorus oxychloride. Prior to the conclusion of the synthesis with olivetol an attempt was made to utilise 4-*n*-hexylresorcinol in a similar manner. The only product isolated from its reaction with the piperidone ester hydrochloride in a sulphuric acid medium was a crystalline *compound* $C_{22}H_{31}O_5NS$; the constitution of this material was not elucidated and this part of the project was abandoned.

Experimental.

A mixture of ethyl *N*-methyl-4-piperidone-3-carboxylate hydrochloride (McElvain, *J. Amer. Chem. Soc.*, 1924, **46**, 1721) (5·5 g.) with resorcinol (3·5 g.) was treated with concentrated sulphuric acid (9 c.c.) in small portions with stirring and cooling and the solution kept for 24 hours; occasionally a sulphate separated after some hours. The mixture was poured into water, neutralised with a slight excess of sodium bicarbonate, and the precipitated mixture of organic and inorganic products collected and extracted (Soxhlet) with chloroform. *7-Hydroxy-3 : 4-(1′-methyl-1′ : 2′ : 5′ : 6′-tetrahydro-3′ : 4′-pyrido)-coumarin* (V) (yield, 25%) separated from the extract. It could be crystallised with some loss from ethanol, when it formed small pale yellow prisms, m. p. 220° (decomp.) (Found : C, 67·45; H, 5·95. $C_{12}H_{12}O_3N$ requires C, 67·5; H, 5·6%); it gave no indophenol reaction. Light absorption (ethanol): max. at λ = 217, 324 mμ; $E^{1\%}_{1cm.}$ = 740, 730. The yield was not improved when phosphorus oxychloride or mixtures with sulphuric acid were used; it deteriorated when the compounds were brought into reaction in any order differing from that above. Methylation of (V) in ether with diazomethane was slow, and a compound of indeterminate constitution was obtained in 30% yield after 10 days at room

temperature; after crystallisation from ethyl acetate it had m. p. 155° (decomp.) (Found: C, 74·2; H, 6·2%). Methylation of (V) was, however, rapid in methanol with ethereal diazomethane, though the reaction was complex. Fractional crystallisation of the mixture from ethyl acetate or methyl cyanide gave three apparently pure materials (described in order of decreasing solubility): the *methyl ether*, which separated from ethyl acetate–ligroin in stout prisms, m. p. 134° (Found: C, 68·65; H, 6·2. $C_{14}H_{15}O_3N$ requires C, 68·55; H, 6·1%); the compound, m. p. 155° (decomp.), obtained previously with diazomethane in ether; and a *compound* which separated from ethanol in pale yellow needles, m. p. 210° (decomp.) (Found: C, 58·5; H, 6·7; N, 4·45. $C_{15}H_{21}O_6N$ requires C, 58·4; H, 6·7; N, 4·5%). Compound (V) (4·2 g.) in pyridine (45 c.c.) was slowly added to a Grignard reagent prepared from magnesium (4·5 g.) and methyl iodide (8 c.c.) in anisole (50 c.c.). After 2 hours on the steam-bath the dark blue product was poured into water (200 c.c.) and acidified with concentrated hydrochloric acid (100 c.c.), residual solid (0·5 g.) being rejected. Anisole was removed in steam, and after addition of sodium carbonate (60 g.) pyridine was likewise removed. The solid was extracted with boiling ethanol (3 lots of 100 c.c.) and the extract concentrated to give the pyran derivative (1·8 g.); *7-hydroxy-3 : 4-(1′-methyl-1′ : 2′ : 5′ : 6′-tetrahydro-3′ : 4′-pyrido)-2 : 2-dimethyl-α-chromen* (VII) separated from ethanol (charcoal) as a pale yellow crystalline powder, m. p. 239° (decomp.) (Found: C, 73·4; H, 7·85. $C_{15}H_{19}O_3N$ requires C, 73·45; H, 7·75%).

4-Imino-3-cyano-1-methylpiperidine (Cook and Reed, *J.*, 1945, 399) (20 g.) was warmed with water (10 c.c.) and concentrated hydrochloric acid (30 c.c.) to effect solution and the whole evaporated to dryness. To it was added resorcinol (16 g.), concentrated sulphuric acid (70 c.c.) and, with stirring, phosphorus oxychloride (50 c.c.). After standing 24 hours, the mixture was poured on to ice and neutralised with sodium bicarbonate. On standing, part of the product separated, and a little more was obtained by extracting the dried salt mixture with pyridine. *5-Hydroxy-3 : 4-(1′-methyl-1′ : 2′ : 5′ : 6′-tetrahydro-3′ : 4′-pyrido)-coumarin* (VI) separated from ethanol in small prisms, m. p. 223°, which gave a strong indophenol reaction (Found: C, 67·9; H, 5·6. $C_{13}H_{13}O_3N$ requires C, 67·5; H, 5·6%); light absorption (ethanol): max. at 218, 324 mμ, E_1^1 = 770, 750. The same compound (0·4 g.) was obtained from 3-cyano-1-methyl-4-piperidone hydrochloride (Cook and Reed, *loc. cit.*) (1·6 g.) and resorcinol (1·1 g.) under similar conditions. Treatment with excess of ethereal diazomethane for 3 days gave the corresponding *methyl ether* in 30% yield; it crystallised from ethanol in needles, m. p. 215°, which depressed the m. p. of the parent compound (Found: C, 68·45; H, 5·9. $C_{14}H_{15}O_3N$ requires C, 68·55; H, 6·1%). Compound (VI) (5 g.) in pyridine (50 c.c.) was added to a Grignard reagent prepared from magnesium (4·3 g.), methyl iodide (10·5 c.c.) and anisole (75 c.c.), at 40° and reaction completed at 65—85° for 16 hours and finally at 100° for 2 hours. A little methanol, 2N-sulphuric acid (100 c.c.) and water (350 c.c.) were added and the solid collected. It was dissolved in 4N-hydrochloric acid (300 c.c.), anisole removed in steam, and the base precipitated with sodium bicarbonate, a little pyridine being then removed in steam. The solid (2·4 g.) was collected, dried and sublimed in a high vacuum at 150° when *5-hydroxy-3 : 4-(1′-methyl-1′ : 2′ : 5′ : 6′-tetrahydro-3′ : 4′-pyrido)-2 : 2-dimethyl-α-chromen* (VIII) (0·5 g.) was collected in microscopic prisms, m. p. 257° (Found: C, 73·0; H, 7·8. $C_{15}H_{19}O_3N$ requires C, 73·5; H, 7·8%).

Orcinol hydrate (5 g.), mixed with ethyl *N*-methyl-4-piperidone-3-carboxylate hydrochloride (7 g.), was treated with cooling with sulphuric acid (16 c.c.) and then with phosphorus oxychloride (6 c.c.). After 24 hours the mixture was poured into excess aqueous sodium bicarbonate and the dried precipitate extracted (Soxhlet) with chloroform. The crude material (5·1 g.) crystallised from butanol or much methyl cyanide and *5-hydroxy-3 : 4-(1′-methyl-1′ : 2′ : 5′ : 6′-tetrahydro-3′ : 4′-pyrido)-7-methylcoumarin* (IX, R = Me) separated in small cubes, m. p. 232° (decomp.) (Found: C, 68·85; H, 6·2. $C_{14}H_{15}O_3N$ requires C, 68·55; H, 6·1%). Compound (IX, R = Me) (4·9 g.) in pyridine (45 c.c.) was slowly added to methylmagnesium iodide (magnesium, 4·5 g., methyl iodide, 11 c.c.) in anisole (70 c.c.) and reaction completed at 65° for 16 hours. 4N-Sulphuric acid was added and anisole removed by distillation in steam; pyridine was similarly removed after adding sodium carbonate and the residue collected. The residue (4 g.) crystallised from butanol and *5-hydroxy-3 : 4-(1′-methyl-1′ : 2′ : 5′ : 6′-tetrahydro-3′ : 4′-pyrido)-2 : 2 : 7-trimethyl-α-chromen hydriodide* separated in rhombic prisms, m. p. 267° (decomp.); it was finally purified by sublimation in high vacuum (Found: C, 49·55; H, 6·0. $C_{16}H_{22}O_3NI$ requires C, 49·6; H, 5·7%).

An intimate mixture of anhydrous olivetol (Anker and Cook, *J.*, 1945, 311) (3·6 g.) and ethyl *N*-methyl-4-piperidone-3-carboxylate hydrochloride (4·5 g.) was treated slowly with concentrated sulphuric acid (10 c.c.) and then with phosphorus oxychloride (2 c.c.) and left for 24 hours. The mixture was decomposed with water and sodium bicarbonate and the whole thoroughly extracted with chloroform. Evaporation of the extract gave *5-hydroxy-3 : 4-(1′-methyl-1′ : 2′ : 5′ : 6′-tetrahydro-3′ : 4′-pyrido)-7-n-amylcoumarin* (IX) (R = C_5H_{11}), which separated from ethyl acetate in prisms, m. p. 170° (yield, 3·7 g.) (Found: C, 71·5; H, 7·65; N, 4·55. $C_{18}H_{23}O_3N$ requires C, 71·75; H, 7·7; N, 4·65%); it gave a strongly positive indophenol reaction. Compound (IX, R = C_5H_{11}) (5 g.) in warm anisole (150 c.c.) was added dropwise to a Grignard reagent prepared from magnesium (3·3 g.), methyl iodide (7·5 c.c.) and anisole (45 c.c.); heat was evolved and the reaction was completed at 85° for 2 hours. Anisole was removed in steam after adding water and a large volume of 4N-sulphuric acid; the dried mixture of salts was extracted thoroughly with ether leaving 5-hydroxy-3 : 4-(1′-methyl-1′ : 2′ : 5′ : 6′-tetrahydro-3′ : 4′-pyrido)-2 : 2-dimethyl-7-*n*-amyl-α-chromen (X, R = C_5H_{11}) as its *hydriodide* (6·5 g.) which separated from ethanol in rectangular plates, m. p. 268° (Found: C, 54·25; H, 6·65. $C_{29}H_{30}O_3NI$ requires, C, 54·2; H, 6·85%). On shaking the hydriodide with aqueous sodium bicarbonate and chloroform the free *base* (X, R = C_5H_{11}) was extracted; it separated from ethyl acetate in octahedra, m. p. 169° (Found: C, 76·0; H, 9·0. $C_{29}H_{29}O_3N$ requires C, 76·2; H, 9·2%).

Compound (X) (R = C_5H_{11}) (4 g.) in acetic acid (50 c.c.) was hydrogenated over Adams' catalyst (0·2 g.) at 13 atm.; the theoretical quantity of hydrogen was absorbed after 90 minutes. Removal of solvent under reduced pressure gave the *acetate* of (XI), which separated from ethyl acetate in rhombic plates (1·2 g.), m. p. 162° (Found: C, 69·9; H, 9·35. $C_{32}H_{35}O_4N$ requires C, 70·0; H, 9·4%); light absorption (ethanol): max. at λ = 280 mμ, E_1^1 = 34·3. The free base was obtained by dissolving the acetate in ethanol (10 c.c.), pouring into 10% aqueous sodium hydroxide (30 c.c.) and introducing an excess of carbon dioxide. *5-Hydroxy-3 : 4-(1′-methyl-1′ : 2′ : 5′ : 6′-tetrahydro-3′ : 4′-pyrido)-2 : 3-dimethyl-7-n-amyl-α-chromen* (XI) crystallised in pale yellow microscopic prisms, m. p. 147°, from ligroin (Found: C, 75·9; H, 9·5. $C_{30}H_{31}O_2N$ requires C, 75·7; H, 9·8%).

A mixture of 4-*n*-hexylresorcinol (8·5 g.), ethyl *N*-methyl-4-piperidone-3-carboxylate (10 g.), sulphuric acid (22 c.c.) and phosphorus oxychloride (7 c.c.), after standing for some hours, was poured into water. The *product* (13 g.) after separating from glycol monomethyl ether had m. p. 218°; it contained N and S but no SO_4 ions (Found: C, 62·7; H 7·35; N, 2·95, 3·35. $C_{22}H_{31}O_5NS$ requires C, 62·7; H, 7·4; N, 3·3%).

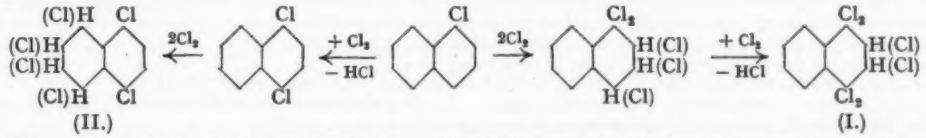
The authors thank Professor I. M. Heilbron, D.S.O., F.R.S., for his interest and encouragement and I.C.I. Ltd. Dyestuffs Division) for grants and gifts of chemicals.

IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY, LONDON, S.W. 7. [*Received, October 15th*, 1945.]

NOTES.

1 : 2 : 3 : 4-*Tetrachloronaphthalene.* By W. PALMER WYNNE.

IN their paper on tetrachloronaphthalenes derived from dichloronaphthalene tetrachlorides, Turner and Wynne (*J.*, 1941, 245) described an isomer (I), m. p. 157°, of Widman's 1 : 4-dichloronaphthalene tetrachloride (II), m. p. 172°, obtained from 1-chloronaphthalene not as was his compound by the passage of chlorine into its solution in chloroform, but from it or its tetrachloride (m. p. 131°) in carbon disulphide solution by saturation with chlorine, preferably in sunlight. Whereas, by interaction with alcoholic sodium hydroxide, Widman's product furnished 1 : 3 : 5 : 8-tetrachloronaphthalene, m. p. 131°, the isomer (I) yielded a tetrachloro-derivative, m. p. 196°, of unknown constitution which at the time was thought to be new. Unfortunately, the fact that von Braun *et al.* (*Ber.*, 1923, **56**, 2337 footnote) had prepared a compound, m. p. 198°, described as 1 : 2 : 3 : 4-tetrachloronaphthalene, from 1′ : 2′ : 3′ : 4′-tetrachlorotetralin was overlooked. By repetition of their method, the identity of the two products has been established. The relationship between (I) and (II) is shown in the scheme



(II.) (I.)

Some details may be added to those very briefly mentioned in von Braun's footnote. In the first place, no specific reference is made to the addition of iodine to the tetralin before exhaustive chlorination; without it, a thick, non-crystallisable syrup is the product. The yield of 1′ : 2′ : 3′ : 4′-tetrachlorotetralin, m. p. 174°, averaged 20 g. from 63 g. of highly purified tetralin. Conversion of the tetrachloro-compound (5 g.) into the dibromo-derivative by the addition of bromine (6 g.) to its solution in boiling carbon disulphide, as prescribed, gave an unsatisfactory product, but in acetic acid at the boiling point for half an hour, a uniform separation of tetrachlorodibromotetralin (2·4 g. from 5 g.) either in flat rhombs with a diagonal extinction or in monoclinic prisms, m. p. 146° (von Braun *et al.*, m. p. 142°), was obtained. When the temperature was raised slowly in the usual way, it melted at *ca.* 135° (decomp.) but, if introduced into the bath at temperatures between 135° and 147°, it remained solid for a short time and only at 146—147° did it melt sharply (Found: C, 28·1; H, 1·4; hal., 70·6. Calc. for $C_{10}H_6Cl_4Br_2$: C, 28·1; H, 1·4; hal., 70·5%). The tetrachloronaphthalene from this source had m. p. 196°, did not depress the m. p. of T. and W.'s product and like the latter, when heated with nitric acid (*d* 1·16) at 210—215° under pressure during not more than 10 minutes, gave an acid the dimethyl ester of which had the m. p. 92° found by Graebe for dimethyl 1 : 2 : 3 : 4-tetrachlorophthalate (*Annalen*, 1905, **340**, 247).

The suggestion that Atterberg and Widman's [δ-] tetrachloronaphthalene, m. p. 141° (*Ber.*, 1877, **10**, 1842) might be identical with the 1 : 2 : 3 : 5-derivative (T. and W., *loc. cit.*, p. 244, footnote; the m. p. 144° in the table on p. 247 is a misprint for 141°) has been confirmed by a repetition of their work. When a solution of 1 : 5-dichloronaphthalene (31 g.) in chloroform was saturated with chlorine, the dichloronaphthalene tetrachloride, m. p. 84° (5·7 g.) and trichloronaphthalene dichloride, m. p. 94° (10·8 g.)—separated by the sparing solubility of the latter in methanol—were obtained and both gave the product, m. p. 141°, by interaction with alcoholic sodium hydroxide. By contrast, when 2 : 6-dichloronaphthalene dissolved in chloroform was saturated with chlorine under comparable conditions, the only product isolated was the substitution derivative, 1 : 2 : 6-trichloronaphthalene, m. p. 92° in small yield (5·3 g. from 47·5 g.; Found: Cl, 45·8. Calc. for $C_{10}H_5Cl_3$: Cl, 46·0%).

The author's thanks are due to Imperial Chemical Industries (Billingham Division) Ltd., for a gift of highly purified tetralin and to Mr. F. C. Baker of this laboratory for help in the experimental work.—UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE. [*Received, October 30th*, 1945.]

Quinolyl Derivatives of* p-*Aminobenzamide. By JOHN H. GORVIN.

THREE p-*aminobenzamidoquinolines* have been prepared by reduction of the corresponding *nitro*-compounds obtained by interaction of *p*-nitrobenzoyl chloride with 5-aminoquinoline, 8-aminoquinoline and 8-amino-6-methoxyquinoline respectively. They have been tested for antimalarial or trypanocidal action by Mr. L. G. Goodwin and Dr. P. B. Marshall, but show no appreciable activity against *Plasmodium gallinaceum* in chicks or *Plasmodium cathemerium* in canaries, or against *Trypanosoma equiperdum* and *Trypanosoma cruzi* in mice. Dr. G. Brownlee of the Wellcome Physiological Research Laboratories has found them to be inactive against streptococcal infections in mice.

Preparation of the p-*Nitrobenzamidoquinolines.*—To a mechanically stirred solution of *p*-nitrobenzoyl chloride (1 mol.) in dry ether was slowly added the appropriate aminoquinoline (1 mol.) dissolved in the same solvent. The precipitated orange-yellow hydrochloride was separated after 30 minutes. It was washed with dry ether and decomposed with aqueous ammonia. The crude product (75—85%) was purified by recrystallisation from glacial acetic acid. In this way were prepared: 5-p-*nitrobenzamidoquinoline*, pale yellow crystalline powder, m. p. 267—268·5° (Found: C, 65·6; H, 3·9; N, 14·2. $C_{16}H_{11}O_3N_3$ requires C, 65·5; H, 3·8; N, 14·2%); 8-p-*nitrobenzamidoquinoline*, small golden needles, m. p. 188° (Found: C, 65·6; H, 3·9; N, 14·4%); 8-p-*nitrobenzamido*-6-*methoxyquinoline*, orange-yellow felted needles, m. p. 241° (Found: C, 63·4; H, 4·5. $C_{17}H_{13}O_4N_3$ requires C, 63·2; H, 4·1%).

Reduction of the p-*Nitrobenzamidoquinolines.*—For the reduction of the 5-isomeride, iron filings (7·5 g.) and 5% aqueous acetic acid (25 c.c.) were warmed to 95° on a water-bath and the nitro-compound (5 g.) added in small portions. After heating for an hour the mixture was made alkaline and filtered. The dry solid residue was extracted with ethanol in a Soxhlet apparatus, and the crude 5-p-*aminobenzamidoquinoline* (2·6 g., 59%) was recrystallised from the same solvent to give prisms, m. p. 264—265° (Found: C, 73·2; H, 5·0. $C_{16}H_{13}ON_3$ requires C, 73·0; H, 5·0%).

The reduction of the other two nitro-compounds was carried out by hydrogenation in glacial acetic acid in presence of Adams's platinum oxide catalyst. The reaction was slow at ordinary temperature and pressure, but proceeded to completion to give 8-p-*aminobenzamidoquinoline*, needles from aqueous ethanol, m. p. 184° (Found: C, 72·7; H, 5·0. $C_{16}H_{13}ON_3$ requires C, 73·0; H, 5·0%) and 8-p-*aminobenzamido*-6-*methoxyquinoline*, needles from aqueous ethanol, m. p. 213—214° (Found: C, 69·7; H, 5·2. $C_{17}H_{15}O_2N_3$ requires C, 69·6; H, 5·2%). Hydrogenation of 5-*p*-nitrobenzamidoquinoline was impeded by the separation of a highly insoluble intermediate compound, m. p. *ca.* 350°.

All m. ps. are corrected.

The author's thanks are due to Mr. J. R. Soar for experimental assistance and to Mr. A. Bennett for the microanalyses.—WELLCOME LABORATORIES OF TROPICAL MEDICINE, LONDON, N.W.1. [*Received, October 20th*, 1945.]

The Diethylaminoalkylation of 9-*Amino*-p-*phenanthroline.* By Rex G. Jacomb and William O. Kermack.

When 9-amino-*p*-phenanthroline (7-amino-6 : 5 : 2′ : 3′-pyridoquinoline), prepared by the method of Haworth and Sykes (*J.*, 1944, 311), was treated with diethylaminoethyl chloride hydrochloride under various conditions, either no reaction took place or a deeply coloured product was obtained from which dilute alkali precipitated no base but strong alkali precipitated a tarry product. It appeared that one of the nuclear nitrogen atoms had reacted yielding quaternary salts. Haworth and Sykes found that the 9-acetamido-*p*-phenanthroline very readily formed a monomethiodide whereas the analogous acetamido-*m*-phenanthroline yielded metho salts only with difficulty. This formation with difficulty of quaternary salts in the *m*-phenanthroline series is in conformity with the fact that, according to E.P. 454525, the amino-*m*-phenanthroline yields diethylaminoalkylamino-*m*-phenanthroline when heated with the appropriate diethylaminoalkyl chloride hydrochloride. Dewar (*J.*, 1944, 619) describes the alkylaminoalkylation of various aromatic amines in toluene solution in presence of sodamide; the application of this method to 9-amino-*p*-phenanthroline avoided the formation of quaternary compounds and gave the desired diethylaminoalkylamino derivatives. By following Dewar's instructions, the yield was poor, much of the unchanged starting material being recovered. An attempt to speed up the reaction by carrying it out in boiling xylene instead of toluene was unsuccessful; at the higher temperature more rapid reaction obviously took place, but a highly coloured product was obtained as in the earlier experiments in the absence of sodamide, and it appeared that quaternary salt formation had again taken place. However, prolonged treatment with extra sodamide and diethylaminoalkyl chloride much improved the yield. In this way were obtained 9-γ-diethylaminopropylamino-*p*-phenanthroline and 9-β-diethylaminoethylamino-*p*-phenanthroline, both oils conveniently isolated and purified through their crystalline 3 : 5-*dinitrobenzoates*. All attempts to obtain such bases by condensing 9-bromo-*p*-phenanthroline and diethylaminoalkylamines were unsuccessful.

9-γ-*Diethylaminopropylamino*-p-*phenanthroline*. 9-Amino-*p*-phenanthroline (2 g.), toluene (30 c.c. distilled and dried over sodium wire), sodamide (0·5 g.) and γ-diethylaminopropyl chloride (1·5 g., freshly distilled in a vacuum) were refluxed in an oil bath for 18 hours with the addition, every 6 hours, of sodamide (0·2 g.) and γ-diethylaminopropyl chloride (0·8 g.) making a total of sodamide (0·9 g.) and γ-diethylaminopropyl chloride (3·1 g.). After standing overnight the mixture was filtered from a small amount of sodium chloride and the filtrate extracted with 15% acetic acid. The red (green fluorescence) extract was made alkaline with 10N-sodium hydroxide solution and extracted with ether. On drying (sodium sulphate) and removal of the ether, the resulting brown oil was kept for ½ hour under reduced pressure at 100° to remove traces of γ-diethylaminopropyl chloride. To a solution of the residual base in alcohol (*ca.* 5 c.c.) was added a saturated alcoholic solution of 3 : 5-dinitrobenzoic acid. The 3 : 5-*dinitrobenzoate* which separated as an oil, crystallised overnight; it was obtained as oblong prisms (5·2 g.), m. p. 172° after repeated crystallisation from hot water. (Dried at 80° in a vacuum over phosphorus pentoxide; found: C, 53·6; H, 4·2; N, 15·1. $C_{19}H_{22}N_4,2C_7H_4O_6N_2,\frac{1}{2}H_2O$ requires C, 53·5; H, 4·4; N, 15·1%. Dried at 120° in vacuum; found: C, 53·80; H, 4·1. $C_{19}H_{22}N_4,2C_7H_4O_6N_2$ requires C, 54·1; H, 4·4%).

9-β-Diethylaminoethylamino-*p*-phenanthroline was prepared similarly from 9-amino-*p*-phenanthroline and β-diethylaminoethyl chloride. The oily product, dissolved in alcohol, was converted into the 3 : 5-*dinitrobenzoate*. It crystallised from hot water as yellow needles, m. p. 173°, and was dried at 80° under reduced pressure over phosphorus pentoxide (Found: C, 49·7; H, 3·7; N, 14·4. $C_{18}H_{22}N_4,3C_7H_4O_6N_2,H_2O$ requires C, 49·3; H, 3·8; N, 14·8%).—Research Laboratory, Royal College of Physicians, Edinburgh. [*Received, November 2nd*, 1945.]

OBITUARY NOTICES.

GUY DUNSTAN BENGOUGH.

1876—1945.

To many, the name of Guy Dunstan Bengough, who died on January 20th, 1945, is familiar as that of a pioneer worker and a leading authority in the field of metallic corrosion; there can be no doubt, however, that at least equal distinction could have been his in fields other than the one he made so much his own.

The son of the late Major E. B. Bengough of Chislehurst, Bengough was born on February 11th, 1876. He was educated at Malvern and at Selwyn College, Cambridge, where he graduated in 1898. Among the subjects in his School and University curricula were botany and zoology, his mastery of which he displayed many years later when presiding over a Committee dealing with the fouling of ships' hulls by marine organisms. He was attracted at an early date to problems associated with metals, and during 1899—1902 studied metallurgy at the Royal School of Mines, following this up with several months in the research laboratory of the Royal Mint under Sir William Roberts-Austen.

Bengough's first appointment (1902—1903) was that of Lecturer in Chemistry and Metallurgy at the Sir John Cass Technical Institute, London, where he started what was to prove a flourishing Department of Metallurgy; he resigned this post to become metallurgist and assayer to a Burmese tin syndicate. On returning to this country he was appointed Lecturer in Metallurgy at Birmingham University under Professor T. Turner; and in 1907 he took charge of the newly-formed Metallurgy Department at Liverpool University. From this point Bengough's career falls into three phases, very unequal and slightly overlapping chronologically, but each characterised by an enthusiastic devotion to a central theme of research.

The first of these phases covers a period of purely metallurgical research, having special reference to the influence of heat-treatment on the structure and mechanical properties of copper and copper–zinc alloys. This work was published in a series of papers (Bengough and co-authors) the last of which appeared in 1914. Here was a fruitful field for further research holding great academic promise bearing in mind Bengough's background of training and experience.

In 1911, however, an event had occurred that was destined to modify profoundly the whole of his subsequent career. The Institute of Metals had already set up a Committee " for the purpose of furthering the study of the causes and prevention of the corrosion of non-ferrous metals and alloys ", particularly under marine conditions; and in that year, at the invitation of the Committee, Bengough presented a report summing up the existing knowledge and setting out a proposed scheme of research. This task served to reveal the general paucity of information inasmuch as most of the previous corrosion research, *e.g.*, by Friend, by Dunstan, and by Moody in this country had been restricted essentially to ferrous corrosion. Bengough was sufficiently attracted to the subject to commence work upon the experimental scheme, and in 1913, in collaboration with R. M. Jones, the results of a preliminary but comprehensive research were published as the Second Report to the Corrosion Research Committee.

Shortly after the outbreak of war in 1914 Bengough was gazetted to the Royal Garrison Artillery, T.F., and in 1915—1916 he was Captain and Adjutant to the C.R.A. Mersey defences. In the latter year, at the request of the Admiralty, following an epidemic of corrosion troubles in the Navy, he was seconded to the Institute of Metals for the purpose of continuing his corrosion researches, with particular reference to condenser tubes. This was now coupled with a definite appointment, the experimental work being transferred from Liverpool University to the Royal School of Mines in London; from this time onwards Bengough was committed to the full-time investigation of metallic corrosion. Subsequent reports (the late W. E. Gibbs had been mainly responsible for the Third Report in 1916) were published in collaboration with O. F. Hudson, R. M. Jones, Miss R. Pirret, J. M. Stuart, and R. May. The whole seven reports, appearing between 1911 and 1924, are impressive monuments in the history of corrosion research; they contain a wealth of information on immersed corrosion, particularly in respect to the nature of surface films of reaction product, and they have led to material advances in corrosion prevention.

In 1924 a change of direction was effected; a new Committee, under the Chairmanship of Professor (later Sir Harold) Carpenter, was set up by the Department of Scientific and Industrial Research for the express purpose of studying corrosion in its more fundamental aspects. Bengough accepted the appointment as Investigator under this Committee, the experimental work at first continuing at the Royal School of Mines. His immediate assignment was, however, an *ad hoc* and eminently practical one on behalf of the Royal Air Force, namely, the development of an improved method of protecting aluminium alloys against corrosion, particularly in aircraft operating in marine atmospheres. This work, in collaboration with J. M. Stuart, resulted in the well-known process of anodic oxidation associated with the names of these workers. The process, which has come into use all over the world wherever aircraft are made, besides being applied to many other diverse purposes, has been used on an enormous scale during the second world war.

The implementation of the new programme of fundamental research became possible with the building, in 1927, of the Department's Chemical Research Laboratory at Teddington, in which appropriate accommodation and facilities were allocated for this purpose by the Director, Professor G. T. (later Sir Gilbert) Morgan, to whom Bengough, as Principal Scientific Officer, acted as Deputy. The new programme involved no less

than a complete change of outlook towards corrosion research. It had become clear to Bengough, as he emphasized on many occasions, that corrosion, hitherto regarded as a matter essentially for the metallurgist, was much more truly the territory of the chemist, and that many of the problems awaiting solution were amenable to the technique of modern physical chemistry. Experimental work was commenced early in 1928, with the support of a team of workers, including J. M. Stuart, A. R. Lee, F. Wormwell, and Miss R. Pirret, all of whom Bengough inspired with his own unbounded enthusiasm. There followed a series of investigations that can truly be said to have raised corrosion research to a level hitherto untouched in respect of accuracy of measurement, degree of control and elegance of detail. Quantitative experiments under strictly defined and reproducible conditions aimed primarily at the discovery of the factors that control corrosion rates under conditions of complete immersion. Especial importance was attached to the establishment of long-continued corrosion/time curves of known reproducibility; such curves, and their response to artificially controlled modifications of environment, supplemented by detailed observations and photographic records of the distribution of corrosion, enabled important conclusions to be reached as to the mechanism of the corrosion process. The accuracy of the control permitted experiments to be repeated, often after long intervals of time, with practical identity of results.

The general plan of the Teddington researches was that of beginning with the simplest possible conditions and proceeding systematically to conditions of increasing complexity. For example " conductivity " water was used before solutions of simple salts, and these in turn before sea-water; zinc was investigated before the multivalent iron notwithstanding the greater industrial importance of the latter; conditions of maximum stagnancy were investigated before conditions of movement, and so on. Up to 1933, the results were published mainly in a series of papers in the *Proceedings of the Royal Society* (" Theory of Metallic Corrosion in the Light of Quantitative Measurements, Parts I to VI "), a series no less noteworthy than Bengough's earlier reports to the Institute of Metals. In 1933, Bengough summarised the results to date in the Third Jubilee Memorial Lecture to the Society of Chemical Industry. Later, with F. Wormwell, he published papers elsewhere principally on the design, interpretation and uses of standard corrosion tests in salt solutions and industrial waters. With L. Whitby, he published work on the protection of magnesium by selenium coatings. The last piece of work with which he was associated at Teddington was the development of the " high-speed rotor apparatus," a direct outcome of fundamental research on the influence of movement; publication of this technique, already long delayed, was withheld for security reasons during the war since it was being employed for a very large number of important service tests. In 1936, Bengough retired from his full-time post at Teddington, but for several years held a temporary part-time appointment which enabled him to keep in touch with the progress of the corrosion work. Yet another cognate sphere of interest outside the Department, however, awaited him.

The subject of marine corrosion, with particular reference to ships' hulls and including fouling due to marine organisms as well as deterioration from corrosion, had been engaging the attention of the Joint Corrosion Committee of the Industrial Research Council and the Iron and Steel Institute, of which Bengough had been a member since its inception. In 1938, a Sub-Committee was formed, with Bengough as Chairman, to cover this field and to arrange for the institution of specific investigations. In spite of the immense economic importance of the fouling problem, in terms of reduced ships' speeds and increased fuel consumption, there was then a comparative dearth of published information and a complete absence of systematic research on this subject by any official body in this country. Bengough threw himself into this new task with all his old enthusiasm, and to him undoubtedly is the major credit of getting together not only a committee representative of various technical and shipping interests on which eminent marine biologists gave of their best, but also a brilliant team of research workers. Under Bengough's inspiring leadership many difficulties were overcome; and already a vast amount of invaluable data has been accumulated and substantial progress in the anti-fouling problem has been made. His last two papers, which he read in 1943, gave a general survey of this work and aroused much interest among marine engineers and naval architects.

Bengough was not merely an efficient chairman; by his visits to the Laboratory of the Scottish Marine Biological Association at Millport (Isle of Cumbrae) where the Committee's experimental anti-fouling work was being carried out, to the Committee's experimental raft off Caernarvon and to various docks for the inspection at first hand of ships' hulls (appraising both the nature of the growths and the efficacies of protective treatments), he played an active and material part in facilitating the Committee's experimental work. These visits—at various times of the year, often in bad weather and always under adverse war-time conditions—made demands upon his health that might well have over-taxed a much younger man. Besides all this, it fell to his lot, as Chairman of the Sub-Committee, to make contacts with outside interests that called for considerable tact and diplomacy; before his death he had the satisfaction of knowing that this—in some respects the most difficult—part of his task was yielding tangibly good results. This last phase of Bengough's career was one that he took very seriously and his passing was immediately and acutely felt by all those associated with the work. He missed only one meeting of his Sub-Committee before his death, and at the last meeting over which he presided he was already suffering from the illness that was to prove fatal.

Bengough received the Cambridge M.A. in 1901 and the Liverpool D.Sc. in 1913. He was elected a Fellow of the Royal Society in 1938. His services to corrosion research were recognised by a " Beilby Award " (Sir George Beilby Memorial Fund) in 1930, and by a Jubilee Memorial Lectureship of the Society of Chemical Industry in 1933. In 1928 he gave a special lecture on corrosion before the 8th Congress of Industrial Chemistry

at Strasbourg; he also wrote the article on corrosion for the latest edition of the *Encyclopædia Britannica*. He served for some years on the Wire Ropes Committee of the Safety in Mines Research Board, and, from the inception of the work in 1942, he was Chairman of the B.S.I. Technical Committee (also of three Sub-Committees) on Boiler Water Tests. He was elected a Fellow of the Chemical Society in 1902 and published a paper in the *Proceedings* in 1908; another (with Stuart and Lee on the routine preparation of low-conductivity water) appeared in the *Journal* in 1927.

Distinguished in presence and in stature—he was 6 ft. 4 in. in height—and with an erect and military bearing, Bengough made an impressive figure. Quietly dignified in manner, he was withal a charming and brilliant conversationalist and an easy and lucid speaker in public. He possessed in marked degree the capacity of detachment and concentration; he could, for example, turn to some literary task, whatever had previously engaged his attention and become immediately impervious to external distractions. His appearances in public were comparatively rare except only at scientific discussions to which he had something definite to contribute. It was largely his highly developed critical faculty that led him not infrequently into controversy. It can be said of him, quoting the words of Samuel Butler, that he " neither expected nor gave quarter in a philosophical argument "; but his own outlook might truly be described by the further words, " we know well that we score more by retracting after we have been deeply committed, than by keeping to our original course when a new light has been presented to us." Bengough was subject over many years to attacks of sciatica which incapacitated him, sometimes, for long periods; from these prolonged absences he would return with his zeal for research unabated. During the last years he was curiously free from these attacks; but his death was preceded by a most painful illness which he endured with characteristic fortitude.

Bengough married in 1908 Constance Helen, second daughter of the late Lt.-Col. Jelf-Sharp of Kincarrathie, by whom he is survived. In his many activities he had the enthusiastic support of Mrs. Bengough, who acted as his secretary during the later war years.

Chemistry is a catholic subject; and whilst most of Bengough's professional life had been devoted to the study of the reactions of metals with their liquid environment—at one time regarded more especially as the province of the metallurgist—this is now generally accepted as a fruitful branch of chemistry. In G. D. Bengough, a distinguished chemist and a distinguished personality has passed but his work and influence will survive.

W. H. J. Vernon.

IDA SMEDLEY MACLEAN.

1877—1944.

Ida Smedley MacLean was born in Birmingham on June 14th, 1877, the second daughter of William T. Smedley, and died on March 2nd, 1944. In 1913 she married Dr. Hugh MacLean, formerly Professor of Medicine in the University of London at St. Thomas's Hospital, who, with their son and daughter, survives her. Until the age of nine she was taught at her home by her mother and then entered the King Edward's High School, Birmingham, with a scholarship. She took the London Matriculation and Intermediate B.Sc. examinations from school, was awarded a Gilchrist Scholarship for three years for an Honours certificate with four distinctions in the Cambridge University Higher Local Examinations, and also gained the school Exhibition.

Ida Smedley was a student at Newnham College in 1896—1899, taking Parts I and II of the Natural Sciences Tripos. She was awarded a Bathurst Scholarship by the College when she left to take up post-graduate work in London as a Research Student at the Central Technical College, where she worked with Professor H. E. Armstrong. Her work on the *Benzylanilinesulphonic Acids and their Derivatives* formed the subject of the thesis presented to the London University for the Doctorate of Science in 1905.

In 1903 she returned to Newnham College as demonstrator in Chemistry, resigning at the end of 1904 to devote herself entirely to research work in the Davy–Faraday Research Laboratory of the Royal Institution, London. Here she completed a research, begun in the Central Technical College, on *Studies of the Origin of Colour Derivatives of Fluorene* (*J.*, 1905, **87**, 1249—1255).

In 1906 Ida Smedley became an assistant lecturer in the Chemical Department of the University of Manchester, the first woman to be appointed on the staff of that department. During the four years in which she held that post she carried out researches on the refractive power of open-chain hydrocarbons containing contiguous ethenoid groups; on the relation between the chemical constitutions and optical properties of aromatic α- and γ-diketones; and on the relative influence of the ketonic and ethenoid linkages on refractive power. An account of this work was published in a series of papers communicated to the Society during the years 1906—1911.

In 1910 she returned to London, holding a Beit Research Fellowship (1910—1914), and began her biochemical work at the Lister Institute of Preventive Medicine, under Professor (later Sir) Arthur Harden, F.R.S., and remained associated with the Institute for the rest of her life, becoming a member of its staff in 1932. After she retired from her official position at the Lister Institute she continued to work there to within a few months of her death, investigating problems for the Colonial Products Research Council.

During the 1914—18 war Ida Smedley MacLean worked for the Ministry of Munitions and the Admiralty

on various problems of national importance, including the large-scale production of acetone from starch by fermentation. In 1918 she became a Fellow of the Institute of Chemistry.

The value of her early work on fat metabolism and fat synthesis was recognised in 1913 by the award of the Ellen Richards Prize, given by the American Association of University Women to the woman making the most outstanding contribution of the year to scientific knowledge. Her final publication appeared as the first of Methuen's Monographs on biochemical subjects, and was entitled "The Metabolism of Fat". Here she summarised, in a succinct manner, her views on a field of work in which she was a recognised master.

(The writer is indebted to one of Dr. Smedley Maclean's chief collaborators, L. C. A. Nunn, for the following brief review of her work on fat metabolism.)

"The problem of fat synthesis from carbohydrates first attracted her attention, and in 1911 she investigated the auto-condensation of crotonaldehyde and proved that a compound containing an unbranched chain of eight carbon atoms was formed. The result of this investigation gave support to the idea that long unbranched fatty-acid chains could be built up by two, or even four, carbon atoms at a time, from such simple molecules as the two-carbon compound, acetaldehyde. This was important, because earlier work had resulted in the formation of branched carbon chains, which are only of rare occurrence in the natural fats. The work was extended to the pyruvic acid series in 1913, in co-operation with Eva Lubrzynska, and led to the building up of fatty acids containing unbranched chains of eight or more carbon atoms. It was probably the general interest in the work of Robison and Harden on the problem of yeast fermentation involving the study of the complex interactions between phosphate and carbohydrate, that led Ida Smedley MacLean to the study of carbohydrate and fat metabolism in yeast, a fruitful research on which she published some 14 papers in the *Biochemical Journal* (1920—1938), in collaboration with E. M. Thomas, D. Hoffert, E. M. Luce, C. G. Daubeney, R. A. McAnally, and L. D. MacLeod.

During the period 1929—1935, in collaboration with M. A. Battie, M. B. S. Pearce, A. P. Ponsford, R. O. Jones, and L. C. A. Nunn, she carried out researches on the oxidation *in vitro* by hydrogen peroxide of long-chain fatty acids (published in 7 papers in the *Biochemical Journal*). The results of this work, whilst confirming that at least some β-oxidation occurred, were of a more far-reaching importance, as they showed that the addition of a cupric catalyst to the mixture of the fatty-acid soap and hydrogen peroxide increased the rate of oxidation to such an extent that, in certain cases, the fatty acid was degraded in the course of a few minutes to the highest state of oxidation, carbon dioxide. The investigation of the intermediates of this action, which it was hoped would be a laboratory model for gaining some knowledge of the biological oxidation of fat, presented great difficulties, and she was occupied with this work almost to the time of her death.

In a later series of researches, published in 7 papers of the *Biochemical Journal* (1938—1941), in collaboration with L. C. A. Nunn, and with E. M. Hume and H. Henderson-Smith on the biological side, Ida Smedley MacLean followed up, on a more biochemical basis, the classical work of G. O. and M. M. Burr on *Fat Deficiency of Rats*. These investigations proved conclusively the earlier work of the Burrs, but extended it in new directions, including the relative effect of many unsaturated acids, together with that of many of their oxidation products; the places of storage and relative concentration in the various organs of the rat, and their effect on the synthesis and storage of the ordinary depot fat. These comprehensive experiments have added in a striking degree to our knowledge of the function of the highly unsaturated fatty acids in the animal body. Among the important conclusions, the essential nature of arachidonic acid and the necessity of linoleic acid in the diet as the possible starting material for the synthesis of this acid were established. Finally, the chemical constitution of arachidonic acid was determined with an extremely small quantity of material. In the later stages of the final work D. E. Dolby and C. L. Arcus were also contributors.

In addition to her many papers in the *Biochemical Journal*, Ida Smedley MacLean published an article in the *Annual Review of Biochemistry* on the 'Phospholipins' and one on 'Fat Synthesis' in the *Ergebnisse der Enzymforschung*."

Chief among her other interests, and second only to her work in biochemistry, the many friends of Ida Smedley MacLean will place the important part she played in the advancement of the professional status of University women. The British Federation of University Women was inaugurated in 1909 during her residence in Manchester, and has owed very much to her as its first secretary and subsequent holder of the offices of treasurer and president. Among the objects of this body were the encouragement of original research by women, better facilities for professional women, the opening of membership of the learned societies to qualified women, and the extension of the franchise to women. In this last connection she stated clearly in her Presidential Address to the Federation:

> "We are banded together as a body of women graduates and, as such, the special quality we have to contribute is not impetuous action, but balanced judgment: to weigh carefully conditions and circumstances, and to think clearly before taking action is a much needed quality in the social life of today."

In 1919 the British Federation and a similar organisation in the United States co-operated in drawing up a constitution for an International Federation of University Women. During the period between the world wars this was extended and included Federations in all the Dominions, and in the majority of the European countries.

Ida Smedley MacLean took a leading part in this wider activity and was one of the chief promoters of that most constructive piece of work of the Federation, the endowment of International Fellowships for original research. During the period 1924—1935, more than £12,000 was paid to holders of these Fellowships by the International Federation and its constituent National Federations.

Among the other objects of the B.F.U.W. in which Ida Smedley MacLean played an active part was the opening of the learned societies to women members. The election of Madame Marie Curie, in 1904, as an Honorary and Foreign Member of the Chemical Society, encouraged women chemists to petition the Council of the Chemical Society for the admission of women to the Fellowship, and a memoral to this effect, signed by nineteen women chemists, was presented to the Council in October of that year by Ida Smedley and the writer.

This was not the first time that the question of admitting women as Fellows had come under the consideration of the Council, for in 1880 Counsel's opinion was taken on the question.*

> Does the Charter of the Society contemplate or permit of the admission of women as Fellows and if so what alteration, if any, is required in the Bye-Laws? The Council were advised that under the Charter women are admissible as Fellows, but when on three occasions (1880, 1888, and 1892) proposals were made to put it into effect no action was taken, the general feeling being that, although there was no objection in principle to the admission of women as Fellows, the case in their favour was not clearly established by any considerable number of applications for the Fellowship and that a change involving so radical an alteration in the policy of the Society, should be recommended by a maximum vote.

In their consideration of the Memorial the Council were advised that

> married women are not eligible for election as Fellows of the Society; that it is extremely doubtful whether the Charter admits of the election of unmarried women as Fellows; that it would not be wise to elect even unmarried women without first applying for a Supplemental Charter, and that the election of women as Associates would be legal after a modification of the Bye-Laws expressly authorising their election. †

An alteration in Bye-Law III extending the privileges of the Associateship to women was proposed by the Council, but rejected by the Fellows.‡

Having received no satisfactory reply to the Memorial, the signatories canvassed personally a number of Fellows of the Chemical Society to obtain their view on the question of the admission of women as Fellows. So large a number of Fellows expressed a favourable opinion, and signed a statement to that effect, that in May 1908 Professor Tilden presented to the Council a petition signed by 312 Fellows, requesting that steps be taken to ascertain the wishes of the Society as a whole regarding the admission of women to the Fellowship of the Society. Acceding to the request of the memorialists, the Council directed the Secretaries to issue a letter, drawn up by the Council, in which arguments on both sides were set forth, requesting each Fellow to consider these, and to express his opinion, on the ballot paper enclosed therewith. 1,758 Papers were returned, of which 1,094 were in favour of admitting women, and 642 against the proposal, whilst 22 were neutral. Two Extraordinary Meetings of Council were devoted solely to the consideration of this report, and it was resolved, by a considerable majority,

> "That in the opinion of this Council it is desirable that at any time, on recommendation of three Fellows of the Society, women be accepted as Subscribers to the Society. Such women Subscribers shall pay an annual fee of 30*s.*, they shall be admitted to all ordinary Meetings of the Society, they shall have the same use of the library as the Fellows, and they shall be supplied with the "Proceedings," "Transactions," and "Annual Reports" of the Society as these are issued." §

This side-door entry for women into the Society did not meet with the approval of the Signatories of the petition, or of the women chemists,‖ only eleven of whom became Subscribers to the Chemical Society during the subsequent eleven years.

In 1920 the Chemical Society obtained a Supplemental Charter giving the power to make certain necessary changes in the Bye-Laws; among the main changes thus effected was the admission of women to the Fellowship, and in view of this fact the Council decided to abolish the class of Lady Subscribers as from December 31st, 1920.¶

At the ordinary scientific meeting of the Society on December 2nd, 1920, Ida Smedley MacLean was the first woman to be formally admitted to the Fellowship; and she was a member of the Council during the period 1931—1934.

M. A. Whiteley.

ALEXANDER KENNETH MILLER

1856—1945.

Dr. Alexander Kenneth Miller died at his home in Manchester on June 19th, 1945, in his 90th year.

In 1876 Miller commenced the study of chemistry under Professor (later Sir) Edward Frankland and later acted as research assistant to Professor (later Sir) Norman Lockyer. Proceeding to Germany in 1880, he spent about two and a half years at the University of Würzburg and continued his studies under such famous men as Wislicenus, Kohlrausch, and Sandberger, and eventually took the degree of Doctor of Philosophy.

On coming back to this country in 1882 Miller was appointed assistant to Professor H. E. Armstrong, and in 1884 was appointed Senior Demonstrator in the Chemical Department of the Central Institution of the City and Guilds of London Technical Institute. During this period he devoted much of his spare time to various aspects of chemical investigation in collaboration with Armstrong and published the results in the Society's *Journal* and in the *Berichte*. Shortly after this, Miller became associated with the well-known firm of F. Bayer & Co., at their branch works near Glasgow, a position which he held until the works were closed in 1890. Later in that year he carried out some important work with Professor T. E. Thorpe, on the colouring matter of alder-bark.

* Council of the Chemical Society, Minutes of the Meetings, 1880, IV, 215, 219; 1881, IV, 221; 1888, V, 103; 1892, V, 212, 226; *P.*, 1893, **9**, 84.
† Council of the Chemical Society, Minutes of the Meetings, VIII, April 21st, 1904; *J.*, 1905, **87**, 538.
‡ *P.*, 1905, **21**, 41—59. § *J.*, 1909, **95**, 614; *P.*, 1908, **24**, 203, 277.
‖ *Nature*, 1908, **78**, 226; 1908, **79**, 37, 399, 429, 488; **80**, 67.
¶ *J.*, 1919, **115**, 388; 1920, **117**, 419; 1921, **119**, 515.

Miller was a Fellow of the Royal Institute of Chemistry, a Fellow of the Chemical Societies of London and Berlin, a member of the Society of Public Analysts, and an original member of the Institute of Brewing. Amongst his published works are studies on dihydroxybenzoic acid, camphor, *m-iso*propyltoluenesulphonic acid, *p*-toluenesulphonic acid, the constitution of benzene, the composition of shale spirit, and Guthrie's compound of amylene with nitrogen peroxide.

Shortly after leaving Thorpe, Miller took the unusual course of abandoning pure organic chemistry for the study of fermentation and became chemist to Messrs. Chester's Brewery, Ltd., of Ardwick, Manchester, who sent him to Copenhagen to study the subject of pure yeast culture under Professor Jörgensen. On his return from Denmark he introduced the use of Hansen's pure culture yeast into the brewery in conjunction with C. F. Hyde and later published his results in the Transactions of the North of England Section of the Institute of Technical Brewing. This is a paper of considerable merit and a very valuable contribution to the technique of top fermentation. Eventually he forsook the purely brewing side and started in practice as a Brewer's Consultant in Manchester, later to join forces with Dr. Hiepe. After the decease of his partner, Miller carried on alone at City Road, Manchester, until he retired in 1934. He was called as an expert witness before the Royal Commission on Arsenical Poisoning and rendered very valuable service.

In addition to being a competent chemist Miller was a man of very modest character and a conscientious, painstaking worker. He was well known in the North of England where his easy personality and charm of manner gained him many friends. As a hobby, he collected clocks and musical boxes of all kinds and had a considerable collection which he was always delighted to show to an interested visitor. His City Road laboratory, now occupied by the writer of this note, contains his comprehensive library and many of his notes and papers which are of absorbing interest.

Miller was the fifth of the six sons of John Miller, the artist (1818—1871); one brother was Keeper of Printed Books at the British Museum, another a portrait painter, while yet another was a well known mezzotint engraver. One of the brothers took a degree at Würzburg University and subsequently worked for some 30 years at the Rothamstead Experimental Station at Harpenden.

In a family in which science and the arts were uniquely blended, Miller was a worthy exponent of the sciences. He lived a full life and enjoyed good health almost to the end which came after a brief illness. He left a widow, two sons, and a daughter.

A. J. Curtin Cosbie.

CLARENCE SMITH.

1875—1945.

Clarence Smith, son of Arthur and Kate Smith (née Carden), was born at Brighton 9th November, 1875, and died at Handcross, Sussex, 28th June, 1945. He was educated at Brighton Grammar School and later at the Royal College of Science, South Kensington, as a Royal Exhibitioner, taking the Associateship with a First Class in Chemistry in 1897 and graduating B.Sc. at London University.

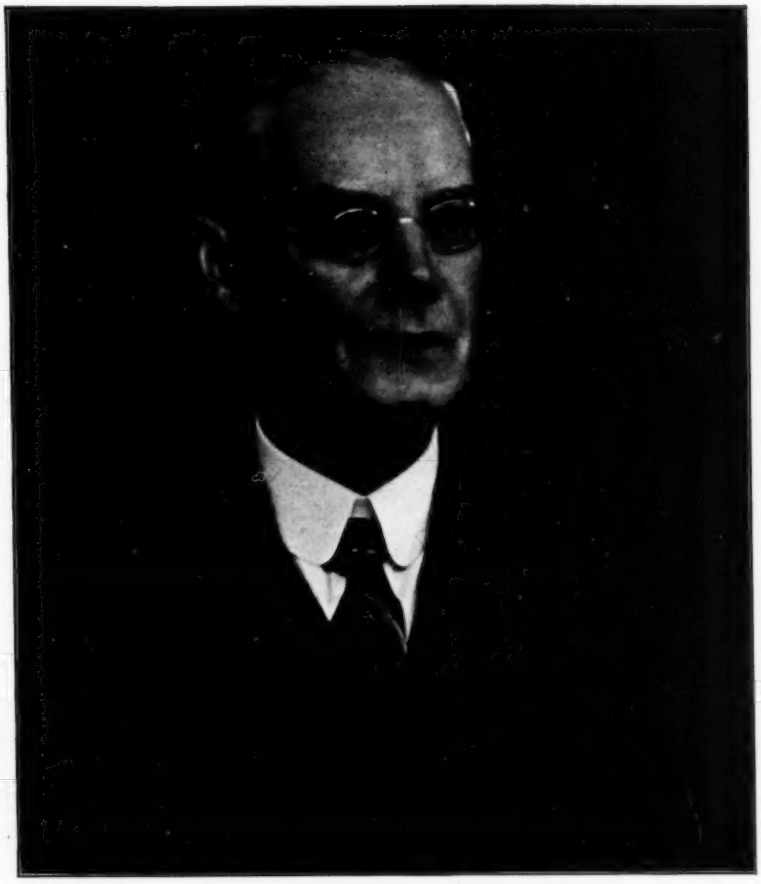
From 1897 to 1899, Smith assisted in teaching Practical Chemistry at the Royal College and then spent two years in school teaching, but returned to the College in 1901 in order to pursue research on certain naphthalene derivatives which gained him the D.Sc. degree in 1903. In writing a testimonial for him at this time, Sir William Tilden remarked that he had " from the first exhibited an excellent combination of ability and industry " and further " he performed all his duties to my entire satisfaction and to the benefit of the students with whom he was brought into contact."

Smith acted as Assistant in the Organic Chemical Laboratory of University College, London, for three months in the Spring of 1903, filling the place of Dr. Smiles who had fallen ill. This entailed giving some lectures on advanced organic chemistry, and Professor Collie remarked that all his work " was done in a most satisfactory manner and he was always ready to help in every way possible."

The present writer became acquainted with Smith in 1903 when he was appointed to the lectureship in Chemistry at East London Technical (now Queen Mary) College; he worked there until 1915. In addition to his teaching duties and research work, he entered into the social life of the College and was always to the fore in helping students in arranging entertainments. In giving Smith a testimonial Principal Hatton wrote " He is possessed of tact and good judgment, which should largely assist him in the discharge of such duties. He has proved himself to be an agreeable colleague and one always willing to take part in the social life of the College." The present writer found a very good friend in Smith and the relationships of the chemical staff were excellent.

The Department of Explosives Supply applied for Smith's services in 1915, whereupon he went to Storey's Gate. The present writer was put in charge of the D.E.S. Laboratory at Chiswick in 1916 and Smith joined him there soon afterwards, acting as deputy when the principal was away. Those were strenuous times, long hours in the laboratory or alternatively travelling about the country visiting factories. Most of Smith's work at Chiswick dealt with high explosives, but he was also called in to test out on pilot-plant scale the manufacture of one of the substances suggested as sternutatory agents. The process, as handed over, was most unpleasant and gave rise to several fires; the use of the particular substance was fortunately abandoned.

From 1919 Smith was engaged with the present writer in managing a small chemical works, and from 1924 he devoted his whole time to the Chemical Society, becoming the Editor of the *Journal* after the death of Dr.



DR. CLARENCE SMITH.

[*To face p.* 68.

J. C. Cain. After the war of 1914—1918, the conditions of the publication of chemical work had undergone a considerable change. The importance of chemistry had received forcible recognition, the number of research workers had largely increased, whilst the costs of publication had gone up. The Chemical Society had " to cut its coat according to its cloth " and steps were taken to keep the length of papers within reasonable bounds.

Under these conditions the work of an Editor was far from easy. The writer of an obituary notice in *Chemistry and Industry* (18th August, 1945) has stated the position very clearly.

" In editing the *Journal of the Chemical Society*, Smith's task, apart from the routine of publication, was to reconcile the policy laid down by the Publication Committee and the advice of referees with the interests of authors, a task frequently difficult, but specially so during several years of financial stringency and recently on account of the meagre allocation of paper for scientific publications. At the meetings of the Committee, Smith was consistently careful to protect the interests of authors and he took endless pains in helping them to meet the requirements of publication; even to the extent of re-writing papers for those who could not or would not reduce them to a length which would allow of their being printed. His ' editorial revision ' was at times the subject of criticism, but it is certain that authors as a body owe much to Clarence Smith, for, of the letters he received after papers had been published, a large majority—90% if memory serves—thanked him for the improvements his help had effected."

Dr. A. D. Mitchell, writing to me after Smith's death, refers to his imperturbability and remarks on his editorial work as follows :

" For nearly 25 years he had to cut papers rigorously owing to pressure on finance. If he slightly over-cut there was at once an indignant protest from the author, whereas if he grossly under-cut nobody would ever have realised it unless it had become flagrant. Yet with this ever-present incentive to take the easy course, he conscientiously slaved to do justice to both authors and the Society, and neither complaints nor hard work ever rattled him."

Dr. Mitchell refers to his " great respect and admiration " for Smith, whilst the notice in Chemistry and Industry concludes with :

" Those who knew him will mourn the passing of a modest, sincere and upright man who commanded their affection and respect."

Smith's own contributions to scientific literature were terminated by the outbreak of war in 1914. Whilst his first work was purely organic, he showed a distinct leaning later to physical chemistry.

Smith's earliest paper (*J.*, 1902, **81**, 900) dealt with the diazoamino-compounds of *ar.*-tetrahydro-β-naphthylamine, the work being carried out at the Royal College of Science. The reduction of β-naphthylamine had been studied by Bamberger and his co-workers (*Ber.*, 1887, **20**, 2195; 1888, **21**, 847, 1112; 1889, **22**, 625; 1890, **23**, 876) and it was stated that the *ar.*-tetrahydro-compound yielded azo-colouring matters if coupled with diazonium salts, though no evidence was adduced. If no diazoamines were formed as intermediate products, it would mean that the *ar.*-base retained its naphthalenoid character, which would be surprising. Smith showed conclusively that diazoamines were the first products of reaction; they were isolated, and decomposed into amines and diazonium salts by cold hydrochloric acid (cf. Meldola and Streatfeild, *J.*, 1887, **51**, 438).

In a later paper (*J.*, 1904, **85**, 728) the bromination of acetyl-*ar.*-tetrahydro-β-naphthylamine was recorded. Two monobromo-derivatives were isolated; on hydrolysis and elimination of the amino-group, each yielded 1-bromotetrahydronaphthalene. Thus the bromine had entered the benzenoid nucleus in ortho- and meta-positions to the acetamido-group.

The action of formaldehyde on the tetrahydro-base was also studied (*ibid.*, p. 732) and a methylene compound, $C_{10}H_{11}N{:}CH_2$, obtained. No tendency to formation of an acridine was observed, the substance again exhibiting benzenoid character.

After appointment at East London College, Smith discovered an interesting case of steric hindrance amongst naphthalene derivatives (*J.*, 1906, **89**, 1505). Naphthylamines usually couple with diazonium salts to give aminoazo-colouring matters directly, but Witt (*Ber.*, 1888, **21**, 3483) had found an exception in the case of 2-naphthylamine-8-sulphonic acid. Smith thought this might be due to steric hindrance and confirmed his supposition by showing that, though isomerisation was impossible when position 8 was occupied by a sulphonic group, the smaller nitro-group allowed the diazoamine first produced to be isomerised. Correspondingly, 2-dimethylaminonaphthalene-8-sulphonic acid does not react with diazonium salts, and whilst 1-bromo-β-naphthol couples with diazonium salts with elimination of halogen (Hewitt and H. V. Mitchell), yet 1-bromo-β-naphthol-8-sulphonic acid is unreactive.

In order to throw light on the structure of the hydroxyazo-compounds, Smith and A. D. Mitchell examined their behaviour towards diazomethane and mercuric acetate. With compounds of the benzene series, results were obtained consistent with the hydroxyazo- (not quinonehydrazone) structure for compounds of the para-series; in the ortho-series the results were in some cases negative but not inconsistent with hydroxyazo-structure, and evidence in favour of quinonehydrazones was not obtained (*J.*, 1908, **93**, 842).

The work was extended to the naphthalene series (*J.*, 1909, **95**, 1430) and the compounds obtained by coupling diazotised aniline with α-naphthol and its 2- and 4-nitro-derivatives as well as β-benzeneazo-α-naphthol were examined. With unsubstituted benzeneazo-α-naphthol, only oxidation was observed, but the other compounds gave monomercuri-acetate derivatives. Attempts at determining the orientation of the entrant groups were unsuccessful and azo-compounds from 2 : 4 : 6-tribromoaniline were not subjected to mercuration.

The structure of the diazoamines has been the subject of several researches. As is well known, if a mixed

compound is prepared from two different amines by diazotising one of them and coupling with the other, the order in which they are taken is indifferent, the same compound resulting in each case. Further, if decomposed by warming with acids, two phenols and two bases are generally obtained. Explanations have been sought on two hypotheses : (*a*) two structurally possible diazoamines unite to form a compound, (*b*) the diazoamine has a structure intermediate between the two " canonical " forms. Smith and Miss C. H. Watts (*J.*, 1910, **97**, 562) prepared ethyl derivatives by diazotising *m*- and *p*-nitroanilines and coupling with *p*- and *m*-nitroethylanilines respectively. Two distinct compounds were obtained; their absorption spectra were measured, and a melting-point curve showed that no combination took place when they were mixed.

The subject of pyrogenic decomposition was taken up by Smith and Lewcock; interesting results were obtained with benzene, but the work had to be broken off (*J.*, 1912, **101**, 1061).

The last-named authors (*Ber.*, 1912, **45**, 2358) gave an ingenious confirmation of Aschan's interpretation of the Hell-Volhard reaction, *viz.*, that enolisation precedes bromination (*ibid.*, 1913). Whilst *iso*butyryl chloride should give bromo*iso*butyryl bromide, chloro*iso*butyryl chloride should not react. This was found to be the case.

Two papers (J. C. Cain, J. L. Simonsen, and C. Smith, *J.*, 1913, **103**, 1035; 1914, **105**, 1335) were occasioned by a continuation of the research of the first two authors on the constitution of santalin.

Most of Smith's work dealt with organic chemical problems, but he also branched out in other directions. With A. D. Mitchell (*J.*, 1909, **95**, 2198) a method was given for the volumetric estimation of sulphates with use of ammonium dichromate in place of the procedure described by Precht.

The same authors also dealt with the question of the possible existence of racemic compounds in the liquid state (*J.*, 1913, **103**, 489). The Eotvös–Ramsay–Shields constant (2·12) was measured for *d*-pinene (2·36), *l*-pinene (2·32), *i*-pinene (2·35), and a mixture of *d*- and *l*-pinenes (2·33). Similar results were obtained with the limonenes and methyl *d*-tartrate and racemate. The work was subsequently extended to include aliphatic alcohols, but again no evidence of liquid racemic compounds was obtained (*J.*, 1914, **105**, 1073).

In an interesting paper (*Proc. Roy. Soc.*, 1912, *A*, **87**, 366), Smith stated that all substances should have the same refractive indexes at their respective critical points. Guye (*Ann. Chim. Phys.*, 1906, **21**, 206) showed that for any substance $b(n^2 + 2)d/(n^2 - 1)M = \text{const.}$ (b is Van der Waals's constant). From Traube's calculations this constant has the value 4·03, and assuming that the specific refractivity is constant for all temperatures up to the critical point, then elimination of d_c (critical density $= \frac{1}{3}b$) gives $n_c = 1{\cdot}126$. It was found that the difference from the experimental results was under 1% for most substances; greater differences were not numerous but occurred mostly amongst aromatic compounds and halogen-containing substances.

It was hoped to go into this subject more thoroughly, but the trouble of 1914 intervened. It may be added that the relationship has twice since been rediscovered—once in France and once in Germany if the present writer's memory is not at fault.

Smith also interested himself in several industrial questions, but details are not available.

In 1936, Smith gave a lecture to the Chemical Society on " Modern Chemical Nomenclature " (see *J.*, 1936, 1067). This was in response to a request from the Institute of Chemistry, and a large number of chemists from many societies attended. In his usual clear-minded manner, Smith gave a reasoned statement of the fundamental principles of this difficult subject and, in the opinion of at least one distinguished chemist, it constituted an outstanding contribution to the *Journal*.

In 1906 Smith married Winifred Emma, daughter of James Hobbs of Brighton; she died in 1940 after several years of ill-health which (to quote from a letter) " never drew a complaint from her." He is survived by a daughter, who acted (and still acts) as Editor's Secretary. His son, a Chartered Surveyor by profession, greatly over-worked for the Ministry of Works during the war, besides doing much in the way of Home Guard and fire-watching duties; he was in a sanatorium at the time of Smith's death, and died on October 27th, 1945.

Smith enjoyed society, games, the open air, and the country. He was in his earlier days a fine player at most forms of ball games, " particularly tennis, which he played very well at the age of 60! " (A. D. M.)—in fact for the First Team of his Club. He also was a great chess player.

As a student at the Royal College of Science, Smith made the daily journey between Brighton and Victoria, and after his appointment at East London College he spent most week-ends at Brighton, using a motor-bicycle; this ceased when he married and became a householder.

For some years he lived in Croydon but moved to Staplefield just before the outbreak of war in 1939. His mother and two sisters lived there; the former died early in 1944 at the age of 94.

Recently Smith and his daughter found a house (dated 1676) near Handcross, Sussex, in a remote spot where they got dwelling and garden " in fine condition " (A. D. M.) and were living very happily. Smith enjoyed extremely good health, never having had a doctor in his life, although I believe he did find the extra responsibility of carrying on the work of the *Journal* during this war, without the assistance of the Publication Committee, rather a strain—perhaps more than even he realised. A few days before he died he complained of very bad indigestion and spent the week-end in bed. On the morning of the 28th June, he thought he had a touch of lumbago. In the evening he felt much better and went for a short walk. His daughter found him a few yards from their gate; the cause of his death was angina.

The Chemical Society has lost a most efficient editor and those who knew him a good friend, whilst he will be gratefully remembered by many of his old students.

J. T. Hewitt.

B.D.H

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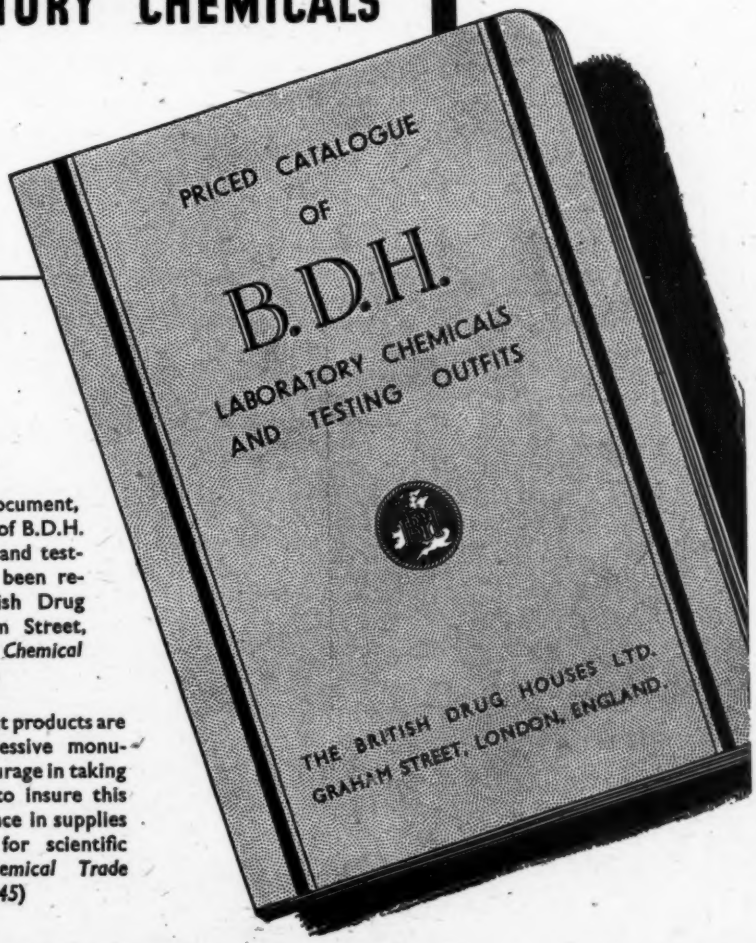

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